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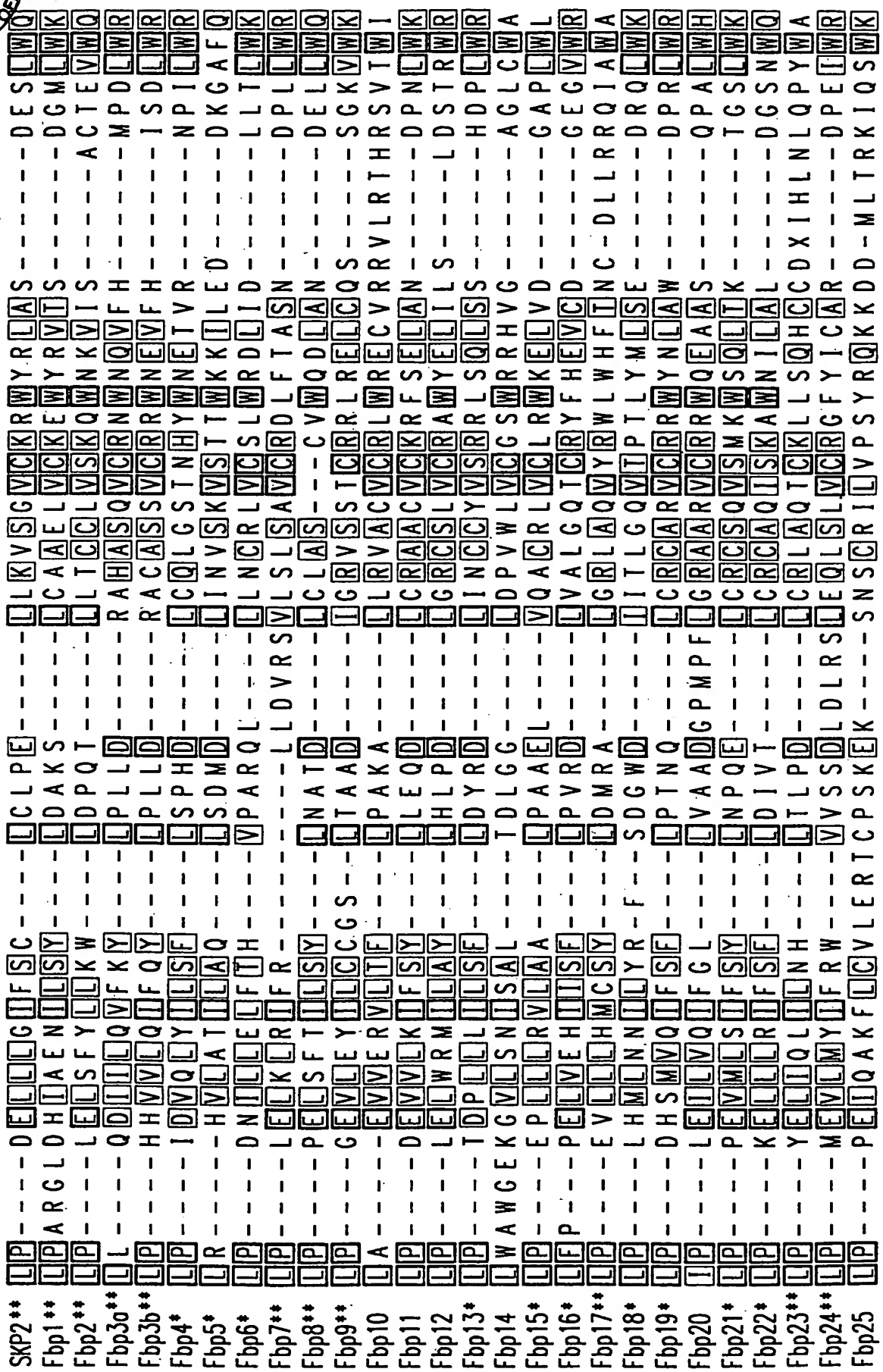
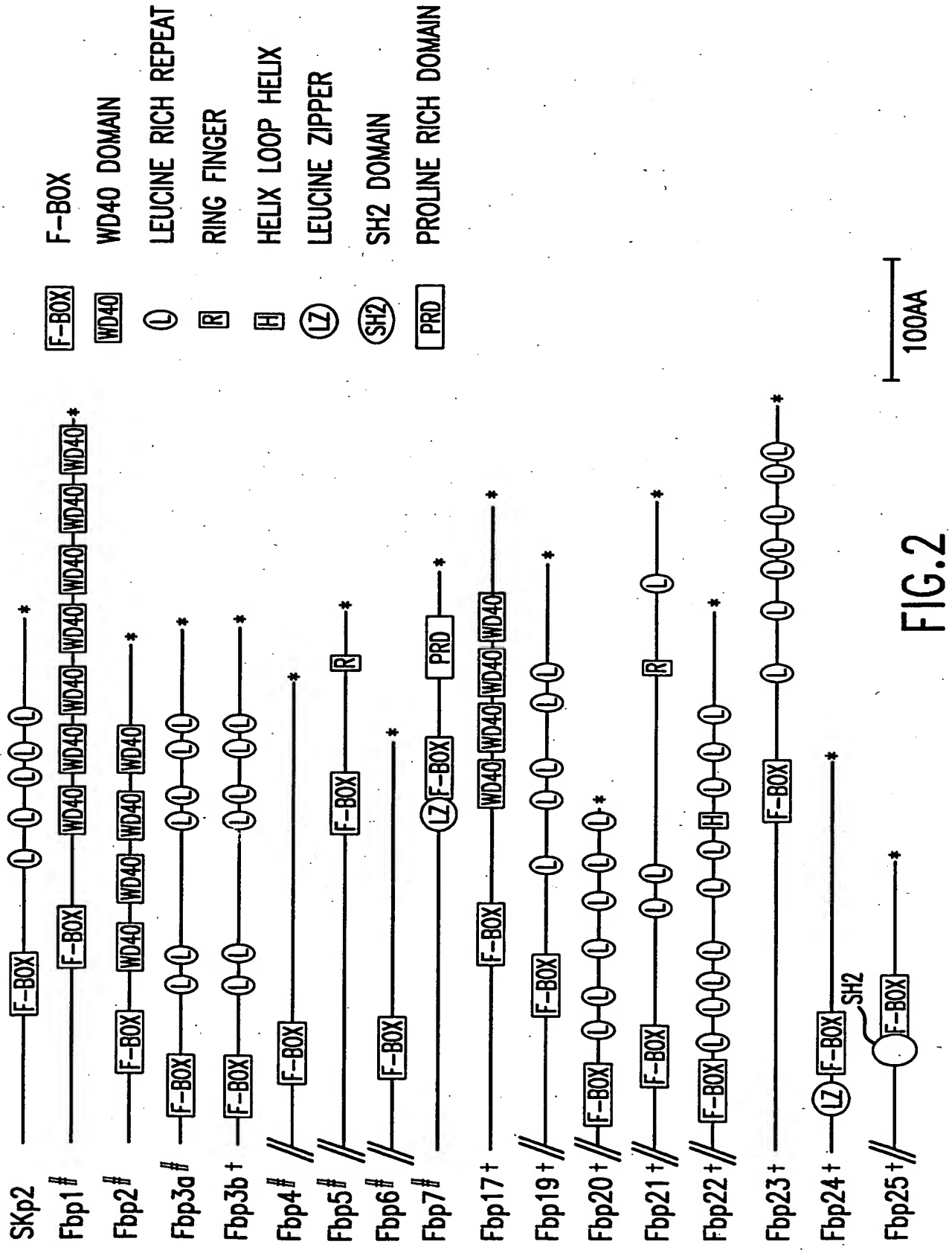


FIG.1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PRD
PROLINE RICH DOMAIN
100AA
Skp2
Fbp1#
Fbp2#
Fbp3a#
Fbp3b+
Fbp4#
Fbp5#
Fbp6#
Fbp7#
Fbp17+
Fbp19+
Fbp20+
Fbp21+
Fbp22+
Fbp23+
Fbp24+
Fbp25+

FIG.2

```
        10         20         30         40         50         60
MDPAEAVLQEKALKFMNSSEREDCNNGEPPRKIIPEKNSLRQTYNSCARLCLNQETVCLA

        70         80         90        100        110        120
STAMKTENCVAKTKLANGTSSMIVPKQRKLSASYEKEKELCVKYFEQWSESDQVEFVEHL

       130        140        150        160        170        180
ISQMCHYQHGHINSYLKPMLQRDFITALPARGLDHIAENILSYLDAKSLCAAELVCKEWY

       190        200        210        220        230        240
RVTSDGMLWKKLIERMVRTDSLWRGLAERRGWGQYLFKNKPPDGNAPPNSFYRALYPKII

       250        260        270        280        290        300
QDIETIESNWRCGRHSLQRIHCRSETSKGVYCLQYDDQKIVSGLRDNTIKIWDKNTLECK

       310        320        330        340        350        360
RILTGHTGSVLCLQYDERVIITGSSDSTVRVWDVNTGEMLNTLIHHCEAVLHLRFNNGMM

       370        380        390        400        410        420
VTCSKDRSIAVWDMASPTDITLRRVLVGHRAAVNVVDFDDKYIVSASGDRTIKVWNTSTC

       430        440        450        460        470        480
EFVRTLNGHKRGIACLQYRDRLVVSGSSDNTIRLWDIECGACLRVLEGHEELVRCIRFDN

       490        500        510        520        530        540
KRIVSGAYDGKIKVWDLVAALDPRAPAGTLCLRTLVEHSGRVFRLQFDEFQIVSSSHDDT

       550        560
ILIWDFLNDPAAQAEPPRSPSRTYTYISR
```

FIG.3A

```
        10         20         30         40         50         60         70         80         90
TGCGTTGGCTGCGGCCTGGCACCAAAGGGGCGGCCCCGGCGGAGAGCGGACCCAGTGGCCTCGGCGATTATGGACCCGGCCGAGGCGGTGCTGC

    100        110        120        130        140        150        160        170        180
AAGAGAAGGCACTCAAGTTTATGAATTCCTCAGAGAGAGAAGACTGTAATAATGGCGAACCCCCTAGGAAGATAATACCAGAGAAGAATTCACT

190        200        210        220        230        240        250        260        270        280
TAGACAGACATACAACAGCTGTGCCAGACTCTGCTTAAACCAAGAAACAGTATGTTTAGCAAGCACTGCTATGAAGACTGAGAATTGTGTGGCC

     290        300        310        320        330        340        350        360        370
AAAACAAAACTTGCCAATGGCACTTCCAGTATGATTGTGCCCAAGCAACGGAAACTCTCAGCAAGCTATGAAAAGGAAAAGGAACTGTGTGTCA

 380        390        400        410        420        430        440        450        460        470
AATACTTTGAGCAGTGGTCAGAGTCAGATCAAGTGGAATTTGTGGAACATCTTATATCCCAAATGTGTCATTACCAACATGGGCACATAAACTC

        480        490        500        510        520        530        540        550        560
GTATCTTAAACCTATGTTGCAGAGAGATTTCATAACTGCTCTGCCAGCTCGGGGATTGGATCATATCGCTGAGAACATTCTGTCATACCTGGAT

    570        580        590        600        610        620        630        640        650
GCCAAATCACTATGTGCTGCTGAACTTGTGTGCAAGGAATGGTACCGAGTGACCTCTGATGGCATGCTGTGGAAGAAGCTTATCGAGAGAATGG

660        670        680        690        700        710        720        730        740        750
TCAGGACAGATTCTCTGTGGAGAGGCCTGGCAGAACGAAGAGGATGGGGACAGTATTTATTCAAAAACAAACCTCCTGACGGGAATGCTCCTCC

     760        770        780        790        800        810        820        830        840
CAACTCTTTTTATAGAGCACTTTATCCTAAAATTATACAAGACATTGAGACAATAGAATCTAATTGGAGATGTGGAAGACATAGTTTACAGAGA

 850        860        870        880        890        900        910        920        930        940
ATTCACTGCCGAAGTGAAACAAGCAAAGGAGTTTACTGTTTACAGTATGATGATCAGAAAATAGTAAGCGGCCTTCGAGACAACACAATCAAGA
```

FIG.3B

950 960 970 980 990 1000 1010 1020 1030
TCTGGGATAAAAACACATTGGAATGCAAGCGAATTCTCACAGGCCATACAGGTTCAGTCCTCTGTCTCCAGTATGATGAGAGAGTGATCATAAC

1040 1050 1060 1070 1080 1090 1100 1110 1120
AGGATCATCGGATTCCACGGTCAGAGTGTGGGATGTAAATACAGGTGAAATGCTAAACACGTTGATTCACCATTGTGAAGCAGTTCTGCACTTG

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
CGTTTCAATAATGGCATGATGGTGACCTGCTCCAAAGATCGTTCCATTGCTGTATGGGATATGGCCTCCCCAACTGACATTACCCTCCGGAGGG

1230 1240 1250 1260 1270 1280 1290 1300 1310
TGCTGGTCGGACACCGAGCTGCTGTCAATGTTGTAGACTTTGATGACAAGTACATTGTTTCTGCATCTGGGGATAGAACTATAAAGGTATGGAA

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
CACAAGTACTTGTGAATTTGTAAGGACCTTAAATGGACACAAACGAGGCATTGCCTGTTTGCAGTACAGGGACAGGCTGGTAGTGAGTGGCTCA

1420 1430 1440 1450 1460 1470 1480 1490 1500
TCTGACAACACTATCAGATTATGGGACATAGAATGTGGTGCATGTTTACGAGTGTTAGAAGGCCATGAGGAATTGGTGCGTTGTATTCGATTTG

1510 1520 1530 1540 1550 1560 1570 1580 1590
ATAACAAGAGGATAGTCAGTGGGGCCTATGATGGAAAAATTAAAGTGTGGGATCTTGTGGCTGCTTTGGACCCCCGTGCTCCTGCAGGGACACT

1600 1610 1620 1630 1640 1650 1660 1670 1680 1690
CTGTCTACGGACCCTTGTGGAGCATTCCGGAAGAGTTTTTCGACTACAGTTTGATGAATTCCAGATTGTCAGTAGTTCACATGATGACACAATC

FIG.3C

1700 1710 1720 1730 1740 1750 1760 1770 1780
CTCATCTGGGACTTCCTAAATGATCCAGCTGCCCAAGCTGAACCCCCCCCGTTCCCCTTCTCGAACATACACCTACATCTCCAGATAAATAACCA

1790 1800 1810 1820 1830 1840 1850 1860 1870 1880
TACACTGACCTCATACTTGCCCAGGACCCATTAAAGTTGCGGTATTTAACGTATCTGCCAATACCAGGATGAGCAACAACAGTAACAATCAAAC

1890 1900 1910 1920 1930 1940 1950 1960 1970
TACTGCCCAGTTTCCCTGGACTAGCCGAGGAGCAGGGCTTTGAGACTCCTGTTGGGACACAGTTGGTCTGCAGTCGGCCCAGGACGGTCTACTC

1980 1990 2000 2010 2020 2030 2040 2050 2060
AGCACAACTGACTGCTTCAGTGCTGCTATCAGAAGATGTCTTCTATCAATTGTGAATGATTGGAACTTTTAAACCTCCCCTCCTCTCCTCCTTT

2070 2080 2090 2100 2110 2120 2130 2140 2150
CACCTCTGCACCTAGTTTTTTCCCATTGGTTCCAGACAAAGGTGACTTATAAATATATTTAGTGTTTTGCCAGAAAAAAAAAA

FIG.3D

```
        10         20         30         40         50         60
MERKDFETWLDNISVTFLSLTDLQKNETLDHLISLSGAVQLRHLSNNLETLLKRDFLKLL

        70         80         90        100        110        120
PLELSFYLLKWLDPQTLLTCCLVSKQWNKVISACTEVWQTACKNLGWQIDDSVQDALHWK

       130        140        150        160        170        180
KVYLKAILRMKQLEDHEAFETSSLIGHSARVYALYYKDGLLCTGSDDLSAKLWDVSTGQC

       190        200        210        220        230        240
VYGIQTHTCAAVKFDEQKLVTGSFDNTVACWEWSSGARTQHFRGHTGAVFSVDYNDELDI

       250        260        270        280        290        300
LVSGSADFTVKVWALSAGTCLNTLTGHTEWVTKVVLQKCKVKSLLHSPGDYILLSADKYE

       310        320        330        340        350        360
IKIWPIGREINCKCLKTLSVSEDRSICLQPRLHFDGKYIVCSSALGLYQWDFASYDILRV

       370        380        390        400        410        420
IKTPEIANLALLGFGDIFALLFDNRYLYIMDLRTESLISRWPLPEYRESKRGSSFLAGEH
```

PG

FIG.4A

```
        10         20         30         40         50         60         70         80         90
ATGGAGAGAAAGGACTTTGAGACATGGCTTGATAACATTTCTGTTACATTTCTTTCTCTGACGGACTTGCAGAAAAATGAAACTCTGGATCACC

    100        110        120        130        140        150        160        170        180
TGATTAGTCTGAGTGGGGCAGTCCAGCTCAGGCATCTCTCCAATAACCTAGAGACTCTCCTCAAGCGGGACTTCCTCAAACTCCTTCCCCTGGA

190        200        210        220        230        240        250        260        270        280
GCTCAGTTTTTATTTGTTAAAATGGCTCGATCCTCAGACTTTACTCACATGCTGCCTCGTCTCTAAACAGTGGAATAAGGTGATAAGTGCCTGT

      290        300        310        320        330        340        350        360        370
ACAGAGGTGTGGCAGACTGCATGTAAAAATTTGGGCTGGCAGATAGATGATTCTGTTCAGGACGCTTTGCACTGGAAGAAGGTTTATTTGAAGG

 380        390        400        410        420        430        440        450        460        470
CTATTTTGAGAATGAAGCAACTGGAGGACCATGAAGCCTTTGAAACCTCGTCATTAATTGGACACAGTGCCAGAGTGTATGCACTTTACTACAA

        480        490        500        510        520        530        540        550        560
AGATGGACTTCTCTGTACAGGGTCAGATGACTTGTCTGCAAAGCTGTGGGATGTGAGCACAGGGCAGTGCGTTTATGGCATCCAGACCCACACT

    570        580        590        600        610        620        630        640        650
TGTGCAGCGGTGAAGTTTGATGAACAGAAGCTTGTGACAGGCTCCTTTGACAACACTGTGGCTTGCTGGGAATGGAGTTCCGGAGCCAGGACCC

660        670        680        690        700        710        720        730        740        750
AGCACTTTCGGGGGCACACGGGGGCGGTATTTAGCGTGGACTACAATGATGAACTGGATATCTTGGTGAGCGGCTCTGCAGACTTCACTGTGAA

      760        770        780        790        800        810        820        830        840
AGTATGGGCTTTATCTGCTGGGACATGCCTGAACACACTCACCGGGCACACGGAATGGGTCACCAAGGTAGTTTTGCAGAAGTGCAAAGTCAAG

 850        860        870        880        890        900        910        920        930        940
TCTCTCTTGCACAGTCCTGGAGACTACATCCTCTTAAGTGCAGACAAATATGAGATTAAGATTTGGCCAATTGGGAGAGAAATCAACTGTAAGT
```

FIG.4B

```
       950        960        970        980        990       1000       1010       1020       1030
GCTTAAAGACATTGTCTGTCTCTGAGGATAGAAGTATCTGCCTGCAGCCAAGACTTCATTTTGATGGCAAATACATTGTCTGTAGTTCAGCACT

  1040       1050       1060       1070       1080       1090       1100       1110       1120
TGGTCTCTACCAGTGGGACTTTGCCAGTTATGATATTCTCAGGGTCATCAAGACTCCTGAGATAGCAAACTTGGCCTTGCTTGGCTTTGGAGAT

1130       1140       1150       1160       1170       1180       1190       1200       1210       1220
ATCTTTGCCCTGCTGTTTGACAACCGCTACCTGTACATCATGGACTTGCGGACAGAGAGCCTGATTAGTCGCTGGCCTCTGCCAGAGTACAGGG

    1230       1240       1250       1260       1270       1280       1290       1300       1310
AATCAAAGAGAGGCTCAAGCTTCCTGGCAGGCGAACATCCTGGCTGAATGGACTGGATGGGCACAATGACACGGGCTTGGTCTTTGCCACCAGC

1320       1330       1340       1350       1360       1370       1380       1390       1400       1410
ATGCCTGACCACAGTATTCACCTGGTGTTGTGGAAGGAGCACGGCTGACACCATGAGCCACCACCGCTGACTGACTTTGGGTGCCGGGGCTGCG

      1420       1430       1440       1450       1460       1470
GGTTTTGGGTGCACCTCTGCGGCACGCGACTGCATGAACCAAAGTTCTCACCTAATGGTATCATCA
```

FIG.4C

```
        10         20         30         40         50         60
MKRGGRDSDRNSSEEGTAEKSKKLRTTNEHSQTCDWGNLLQDIILQVFKYLPLLDRAHAS

        70         80         90        100        110        120
QVCRNWNQVFHMPDLWRCFEFELNQPATSYLKATHPELIKQIIKRHSNHLQYVSFKVDSS

       130        140        150        160        170        180
KESAEAACDILSQLVNCSLKTLGLISTARPSFMDLPKSHFISALTVVFVNSKSLSSLKID

       190        200        210        220        230        240
DTPVDDPSLKVLVANNSDTLKLLKMSSCPHVSPAGILCVADQCHGLRELALNYHLLSDEL

       250        260        270        280        290        300
LLALSSEKHVRLEHLRIDVVSENPGQTHFHTIQKSSWDAFIRHSPKVNLVMYFFLYEEEF

       310        320        330        340        350        360
DPFFRYEIPATHLYFGRSVSKDVLGRVGMTCPRLVELVVCANGLRPLDEELIRIAERCKN

       370        380        390        400        410        420
LSAIGLGECEVSCSAFVEFVKMCGGRLSQLSIMEEVLIPDQKYSLEQIHWEVSKHLGRVW

FPDMMPTW
```

FIG.5A

```
        10         20         30         40         50         60         70         80         90
CGGGGTGGTGTGTGGGGGAAGCCGCCCCCGGCAGCAGGATGAAACGAGGAGGAAGAGATAGTGACCGTAATTCATCAGAAGAAGGAACTGCAGA

    100        110        120        130        140        150        160        170        180
GAAATCCAAGAAACTGAGGACTACAAATGAGCATTCTCAGACTTGTGATTGGGGTAATCTCCTTCAGGACATTATTCTCCAAGTATTTAAATAT

190        200        210        220        230        240        250        260        270        280
TTGCCTCTTCTTGACCGGGCTCATGCTTCACAAGTTTGCCGCAACTGGAACCAGGTATTTCACATGCCTGACTTGTGGAGATGTTTTGAATTTG

     290        300        310        320        330        340        350        360        370
AACTGAATCAGCCAGCTACATCTTATTTGAAAGCTACCCATCCAGAGCTGATCAAACAGATTATTAAAAGACATTCAAACCATCTACAATATGT

 380        390        400        410        420        430        440        450        460        470
CAGCTTCAAGGTGGACAGCAGCAAGGAATCAGCTGAAGCAGCTTGTGATATACTATCGCAACTTGTGAATTGCTCTTTAAAAACACTTGGACTT

        480        490        500        510        520        530        540        550        560
ATTTCAACTGCTCGACCAAGCTTTATGGATTTACCAAAGTCTCACTTTATCTCTGCACTGACAGTTGTGTTCGTAAACTCCAAATCCCTGTCTT

    570        580        590        600        610        620        630        640        650
CGCTTAAGATAGATGATACTCCAGTAGATGATCCATCTCTCAAAGTACTAGTGGCCAACAATAGTGATACACTCAAGCTGTTGAAAATGAGCAG

660        670        680        690        700        710        720        730        740        750
CTGTCCTCATGTCTCTCCAGCAGGTATCCTTTGTGTGGCTGATCAGTGTCACGGCTTAAGAGAACTAGCCCTGAACTACCACTTATTGAGTGAT

     760        770        780        790        800        810        820        830        840
GAGTTGTTACTTGCATTGTCTTCTGAAAAACATGTTCGATTAGAACATTTGCGCATTGATGTAGTCAGTGAGAATCCTGGACAGACACACTTCC

 850        860        870        880        890        900        910        920        930        940
ATACTATTCAGAAGAGTAGCTGGGATGCTTTCATCAGACATTCACCCAAAGTGAACTTAGTGATGTATTTTTTTTTATATGAAGAAGAATTTGA
```

FIG.5B

```
      950       960       970       980       990      1000      1010      1020      1030
CCCCTTCTTTCGCTATGAAATACCTGCCACCCATCTGTACTTTGGGAGATCAGTAAGCAAAGATGTGCTTGGCCGTGTGGGAATGACATGCCCT

  1040      1050      1060      1070      1080      1090      1100      1110      1120
AGACTGGTTGAACTAGTAGTGTGTGCAAATGGATTACGGCCACTTGATGAAGAGTTAATTCGCATTGCAGAACGTTGCAAAAATTTGTCAGCTA

1130      1140      1150      1160      1170      1180      1190      1200      1210      1220
TTGGACTAGGGGAATGTGAAGTCTCATGTAGTGCCTTTGTTGAGTTTGTGAAGATGTGTGGTGGCCGCCTATCTCAATTATCCATTATGGAAGA

    1230      1240      1250      1260      1270      1280      1290      1300      1310
AGTACTAATTCCTGACCAAAAGTATAGTTTGGAGCAGATTCACTGGGAAGTGTCCAAGCATCTTGGTAGGGTGTGGTTTCCCGACATGATGCCC

1320      1330      1340      1350      1360      1370      1380      1390      1400
ACTTGGTAAAAACTGCATGATGAATAGCACCTTAATTTCAAGCAAATGTATTATAATTAAAGTTTTATTTGCTGTAAAAAAAAAAAAAAAA
```

FIG.5C

```
        10         20         30         40         50         60
MKRNSLSVENKIVQLSGAAKQPKVGFYSSLNQTHTHTVLLDWGSLPHHVVLQIFQYLPLL
        70         80         90        100        110        120
DRACASSVCRRWNEVFHISDLWRKFEFELNQSATSSFKSTHPDLIQQIIKKHFAHLQYVS
       130        140        150        160        170        180
FKVDSSAESAEAACDILSQLVNCSIQTLGLISTAKPSFMNVSESHFVSALTVVFINSKSL
       190        200        210        220        230        240
SSIKIEDTPVDDPSLKILVANNSDTLRLPKMSSCPHVSSDGILCVADRCQGLRELALNYY
       250        260        270        280        290        300
ILTDELFLALSSETHVNLEHLRIDVVSENPGQIKFHAVKKHSWDALIKHSPRVNVVMHFF
       310        320        330        340        350        360
LYEEEFETFFKEETPVTHLYFGRSVSKVVLGRVGLNCPRLIELVVCANDLQPLDNELICI
       370        380        390        400        410        420
AEHCTNLTALGLSKCEVSCSAFIRFVRLCERRLTQLSVMEEVLIPDEDYSLDEIHTEVSK
       430
YLGRVWFPDVMPLW
```

FIG.6A

```
        10         20         30         40         50         60
ACATTTTCTAATGTTTACAGAATGAAGAGGAACAGTTTATCTGTTGAGAATAAAATTGTCCAGTTGTCA

70         80         90        100        110        120        130
GGAGCAGCGAAACAGCCAAAAGTTGGGTTCTACTCTTCTCTCAACCAGACTCATACACACACGGTTCTT

140        150        160        170        180        190        200
CTAGACTGGGGGAGTTTGCCTCACCATGTAGTATTACAAATTTTTCAGTATCTTCCTTTACTAGATCGG

210        220        230        240        250        260        270
GCCTGTGCATCTTCTGTATGTAGGAGGTGGAATGAAGTTTTTCATATTTCTGACCTTTGGAGAAAGTTT

280        290        300        310        320        330        340
GAATTTGAACTGAACCAGTCAGCTACTTCATCTTTTAAGTCCACTCATCCTGATCTCATTCAGCAGATC

350        360        370        380        390        400        410
ATTAAAAAAGCATTTTGCTCATCTTCAGTATGTCAGCTTTAAGGTTGACAGTAGCGCTGAGTCAGCAGAA

420        430        440        450        460        470        480
GCTGCCTGTGATATACTCTCTCAGCTGGTAAATTGTTCCATCCAGACCTTGGGCTTGATTTCAACAGCC

490        500        510        520        530        540        550
AAGCCAAGTTTCATGAATGTGTCGGAGTCTCATTTTGTGTCAGCACTTACAGTTGTTTTTATCAACTCA

560        570        580        590        600        610        620
AAATCATTATCATCAATCAAAATTGAAGATACACCAGTGGATGATCCTTCATTGAAGATTCTTGTGGCC

630        640        650        660        670        680        690
AATAATAGTGACACTCTAAGACTCCCAAAGATGAGTAGCTGTCCTCATGTTTCATCTGATGGAATTCTT

700        710        720        730        740        750
TGTGTAGCTGACCGTTGTCAAGGCCTTAGAGAACTGGCGTTGAATTATTACATCCTAACTGATGAACTT

760        770        780        790        800        810        820
TTCCTTGCACTCTCAAGCGAGACTCATGTTAACCTTGAACATCTTCGAATTGATGTTGTGAGTGAAAAT

830        840        850        860        870        880        890
CCTGGACAGATTAAATTTCATGCTGTTAAAAAACACAGTTGGGATGCACTTATTAAACATTCCCCTAGA

900        910        920        930        940        950        960
GTTAATGTTGTTATGCACTTCTTTCTATATGAAGAGGAATTCGAGACGTTCTTCAAAGAAGAAACCCCT
```

FIG.6B

970 980 990 1000 1010 1020 1030
GTTACTCACCTTTATTTTGGTCGTTCAGTCAGCAAAGTGGTTTTAGGACGGGTAGGTCTCAACTGTCCT

1040 1050 1060 1070 1080 1090 1100
CGACTGATTGAGTTAGTGGTGTGTGCTAATGATCTTCAGCCTCTTGATAATGAACTTATTTGTATTGCT

1110 1120 1130 1140 1150 1160 1170
GAACACTGTACAAACCTAACAGCCTTGGGCCTCAGCAAATGTGAAGTTAGCTGCAGTGCCTTCATCAGG

1180 1190 1200 1210 1220 1230 1240
TTTGTAAGACTGTGTGAGAGAAGGTTAACACAGCTCTCTGTAATGGAGGAAGTTTTGATCCCTGATGAG

1250 1260 1270 1280 1290 1300 1310
GATTATAGCCTAGATGAAATTCACACTGAAGTCTCCAAATACCTGGGAAGAGTATGGTTCCCTGATGTG

1230
ATGCCTCTCTGG

FIG.6C

```
        10         20         30         40         50         60
MAGSEPRSGTNSPPPPFSDWGRLEAAILSGWKTFWQSVSKDRVARTTSREEVDEAASTLT
        70         80         90        100        110        120
RLPIDVQLYILSFLSPHDLCQLGSTNHYWNETVRNPILWRYFLLRDLPSWSSVDWKSLPY
       130        140        150        160        170        180
LQILKKPISEVSDGAFFDYMAVYLMCCPYTRRASKSSRPMYGAVTSFLHSLIIPNEPRFA
       190        200        210        220        230        240
LFGPRLEQLNTSLVLSLLSSEELCPTAGLPQRQIDGIGSGVNFQLNNQHKFNILILYSTT
       250        260        270        280        290        300
RKERDRAREEHTSAVNKMFSRHNEGDDRPGSRYSVIPQIQKLCEVVDGFIYVANAEAHKR
       310        320        330        340        350        360
HEWQDEFSHIMAMTDPAFGSSGRPLLVLSCISQGDVKRMPCFYLAHELHLNLLNHPWLVQ
       370        380        390        400        410        420
DTEAETLTGFLNGIEWILEEVESKRAR*FSFQILGTETI*NLLLRS*CEYLLSQPTLSCL
       430        440        450        460        470        480
FADRLSFGQL*LLCFLYYFYFLP*INYKKRVSVLVFSPKMNL*TFFW*FLYFLSF*KY*I
L
```

FIG.7A

```
        10         20         30         40         50         60
ATGGCGGGAAGCGAGCCGCGCAGCGGAACAAATTCGCCGCCGCCGCCCTTCAGCGACTGGGGCCGCCTG

70         80         90         100        110        120        130
GAGGCGGCCATCCTCAGCGGCTGGAAGACCTTCTGGCAGTCAGTGAGCAAGGATAGGGTGGCGCGTACG

140        150        160        170        180        190        200
ACCTCCCGGGAGGAGGTGGATGAGGCGGCCAGCACCCTGACGCGGCTGCCGATTGATGTACAGCTATAT

210        220        230        240        250        260        270
ATTTTGTCCTTTCTTTCACCTCATGATCTGTGTCAGTTGGGAAGTACAAATCATTATTGGAATGAAACT

280        290        300        310        320        330        340
GTAAGAAATCCAATTCTGTGGAGATACTTTTTGTTGAGGGATCTTCCTTCTTGGTCTTCTGTTGACTGG

350        360        370        380        390        400        410
AAGTCTCTTCCATATCTACAAATCTTAAAAAAGCCTATATCTGAGGTCTCTGATGGTGCATTTTTTGAC

420        430        440        450        460        470        480
TACATGGCAGTCTATCTAATGTGCTGTCCATACACAAGAAGAGCTTCAAAATCCAGCCGTCCTATGTAT

490        500        510        520        530        540        550
GGAGCTGTCACTTCTTTTTTACACTCCCTGATCATTCCCAATGAACCTCGATTTGCTCTGTTTGGACCA

560        570        580        590        600        610        620
CGTTTGGAACAATTGAATACCTCTTTGGTGTTGAGCTTGCTGTCTTCAGAGGAACTTTGCCCAACAGCT

630        640        650        660        670        680        690
GGTTTGCCTCAGAGGCAGATTGATGGTATTGGATCAGGAGTCAATTTTCAGTTGAACAACCAACATAAA

700        710        720        730        740        750
TTCAACATTCTAATCTTATATTCAACTACCAGAAAGGAAAGAGATAGAGCAAGGGAAGAGCATACAAGT

760        770        780        790        800        810        820
GCAGTTAACAAGATGTTCAGTCGACACAATGAAGGTGATGATCGACCAGGAAGCCGGTACAGTGTGATT

830        840        850        860        870        880        890
CCACAGATTCAAAAACTGTGTGAAGTTGTAGATGGGTTCATCTATGTTGCAAATGCTGAAGCTCATAAA

900        910        920        930        940        950        960
AGACATGAATGGCAAGATGAATTTTCTCATATTATGGCAATGACAGATCCAGCCTTTGGGTCTTCGGGA
```

FIG.7B

970 980 990 1000 1010 1020 1030
AGACCATTGTTGGTTTTATCTTGTATTTCTCAAGGGGATGTAAAAAGAATGCCCTGTTTTTATTTGGCT

1040 1050 1060 1070 1080 1090 1100
CATGAGCTGCATCTGAATCTTCTAAATCACCCATGGCTGGTCCAGGATACAGAGGCTGAAACTCTGACT

1110 1120 1130 1140 1150 1160 1170
GGTTTTTTGAATGGCATTGAGTGGATTCTTGAAGAAGTGGAATCTAAGCGTGCAAGATGATTCTCTTTT

1180 1190 1200 1210 1220 1230 1240
CAGATCTTGGGAACTGAAACCATTTGAAATTTATTACTAAGGTCGTGATGTGAATATTTGCTCAGTCAG

1250 1260 1270 1280 1290 1300 1310
CCCACCTTGTCCTGCCTTTTTGCAGATAGGCTTTCATTTGGACAGCTATAACTGCTGTGTTTTTTATAT

1320 1330 1340 1350 1360 1370 1380
TATTTTTACTTTTTACCATAAATCAATTACAAGAAAAGAGTTTCAGTCCTAGTATTTAGCCCCAAAATG

1390 1400 1410 1420 1430 1440
AACCTTTAAACATTTTTTTGGTAATTTTTATATTTTCTGTCTTTTTAAAAATATTAAATTTTGG

FIG.7C

```
        10         20         30         40         50         60
MSRRPCSCALRPPRCSCSASPSAVTAAGRPRPSDSCKEESSTLSVKMKCDFNCNHVHSGL

        70         80         90        100        110        120
KLVKPDDIGRLVSYTPAYLEGSCKDCIKDYERLSCIGSPIVSPRIVQLETESKRLHNKEN

       130        140        150        160        170        180
QHVQQTLNSTNEIEALETSRLYEDSGYSSFSLQSGLSEHEEGSLLEENFGDSLQSCLLQI

       190        200        210        220        230        240
QSPDQYPNKNLLPVLHFEKVVCSTLKKNAKRNPKVDREMLKEIIARGNFRLQNIIGRKMG

       250        260        270        280        290        300
LECVDILSELFRRGLRHVLATILAQLSDMDLINVSKVSTTWKKILEDDKGAFQLYSKAIQ

       310        320        330        340        350        360
RVTENNNKFSPHASTREYVMFRTPLASVQKSAAQTSLKKDAQTKLSNQGDQKGSTYSRHN

       370        380        390        400        410        420
EFSEVAKTLKKNESLKACIRCNSPAKYDCYLQRATCKREGCGFDYCTKCLCNYHTTKDCS

       430        440
DGKLLKASCKIGPLPGTKKSKKNLRRL
```

FIG.8A

```
        10         20         30         40         50         60         70         80         90
AGGTTGCTCAGCTGCCCCCGGAGCGGTTCCTCCACCTGAGGCAGACACCACCTCGGTTGGCATGAGCCGGCGCCCCTGCAGCTGCGCCCTACGG

    100        110        120        130        140        150        160        170        180
CCACCCCGCTGCTCCTGCAGCGCCAGCCCCAGCGCAGTGACAGCCGCCGGGCGCCCTCGACCCTCGGATAGTTGTAAAGAAGAAAGTTCTACCC

190        200        210        220        230        240        250        260        270        280
TTTCTGTCAAAATGAAGTGTGATTTTAATTGTAACCATGTTCATTCCGGACTTAAACTGGTAAAACCTGATGACATTGGAAGACTAGTTTCCTA

     290        300        310        320        330        340        350        360        370
CACCCCTGCATATCTGGAAGGTTCCTGTAAAGACTGCATTAAAGACTATGAAAGGCTGTCATGTATTGGGTCACCGATTGTGAGCCCTAGGATT

 380        390        400        410        420        430        440        450        460        470
GTACAACTTGAAACTGAAAGCAAGCGCTTGCATAACAAGGAAAATCAACATGTGCAACAGACACTTAATAGTACAAATGAAATAGAAGCACTAG

        480        490        500        510        520        530        540        550        560
AGACCAGTAGACTTTATGAAGACAGTGGCTATTCCTCATTTTCTCTACAAAGTGGCCTCAGTGAACATGAAGAAGGTAGCCTCCTGGAGGAGAA

    570        580        590        600        610        620        630        640        650
TTTCGGTGACAGTCTACAATCCTGCCTGCTACAAATACAAAGCCCAGACCAATATCCCAACAAAAACTTGCTGCCAGTTCTTCATTTTGAAAAA

660        670        680        690        700        710        720        730        740        750
GTGGTTTGTTCAACATTAAAAAAGAATGCAAAACGAAATCCTAAAGTAGATCGGGAGATGCTGAAGGAAATTATAGCCAGAGGAAATTTTAGAC

     760        770        780        790        800        810        820        830        840
TGCAGAATATAATTGGCAGAAAAATGGGCCTAGAATGTGTAGATATTCTCAGCGAACTCTTTCGAAGGGGACTCAGACATGTCTTAGCAACTAT

 850        860        870        880        890        900        910        920        930        940
TTTAGCACAACTCAGTGACATGGACTTAATCAATGTGTCTAAAGTGAGCACAACTTGGAAGAAGATCCTAGAAGATGATAAGGGGGCATTCCAG
```

FIG.8B

950 960 970 980 990 1000 1010 1020 1030
TTGTACAGTAAAGCAATACAAAGAGTTACCGAAAACAACAATAAATTTTCACCTCATGCTTCAACCAGAGAATATGTTATGTTCAGAACCCCAC

1040 1050 1060 1070 1080 1090 1100 1110 1120
TGGCTTCTGTTCAGAAATCAGCAGCCCAGACTTCTCTCAAAAAAGATGCTCAAACCAAGTTATCCAATCAAGGTGATCAGAAAGGTTCTACTTA

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
TAGTCGACACAATGAATTCTCTGAGGTTGCCAAGACATTGAAAAAGAACGAAAGCCTCAAAGCCTGTATTCGCTGTAATTCACCTGCAAAATAT

1230 1240 1250 1260 1270 1280 1290 1300 1310
GATTGCTATTTACAACGGGCAACCTGCAAACGAGAAGGCTGTGGATTTGATTATTGTACGAAGTGTCTCTGTAATTATCATACTACTAAAGACT

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
GTTCAGATGGCAAGCTCCTCAAAGCCAGTTGTAAAATAGGTCCCCTGCCTGGTACAAAGAAAAGCAAAAAGAATTTACGAAGATTGTGATCTCT

1420 1430 1440 1450 1460 1470 1480 1490 1500
TATTAAATCAATTGTTACTGATCATGAATGTTAGTTAGAAAATGTTAGGTTTTAACTTAAAAAAAATTGTATTGTGATTTTCAATTTTATGTTG

1510 1520 1530 1540 1550 1560 1570 1580 1590
AAATCGGTGTAGTATCCTGAGGTTTTTTTCCCCCCAGAAGATAAAGAGGATAGACAACCTCTTAAAATATTTTTACAATTTAATGAGAAAAAGT

1600 1610 1620 1630 1640 1650 1660 1670 1680 1690
TTAAAATTCTCAATACAAATCAAACAATTTAAATATTTTAAGAAAAAAGGAAAAGTAGATAGTGATACTGAGGGTAAAAAAAAAATTGATTCAA

1700 1710 1720 1730 1740 1750 1760 1770 1780
TTTTATGGTAAAGGAAACCCATGCAATTTTACCTAGACAGTCTTAAATATGTCTGGTTTTCCATCTGTTAGCATTTCAGACATTTTATGTTCCT

1790 1800 1810 1820 1830 1840 1850 1860 1870 1880
CTTACTCAATTGATACCAACAGAAATATCAACTTCTGGAGTCTATTAAATGTGTTGTCACCTTTCTAAAGCTTTTTTTCATTGTGTGTATTTCC

1890 1900 1910 1920 1930 1940 1950 1960 1970
CAAGAAAGTATCCTTTGTAAAAACTTGCTTGTTTTCCTTATTTCTGAAATCTGTTTTAATATTTTTGTATACATGTAAATATTTCTGTATTTTT

1980 1990 2000 2010 2020 2030 2040 2050 2060
TATATGTCAAAGAATATGTCTCTTGTATGTACATATAAAAATAAATTTTGCTCAATAAAATTGTAAGCTTAAAAAAAAAAAAAAAAAAACTCGAG

2070
ACTAGTGC

FIG.8C

```
        10         20         30         40         50         60
ARSGASALRRRRVQVWVLSRPPPGGGDSFRTRRPQRGPGPGGSQAMDAPHSKAALDSINE

        70         80         90        100        110        120
LPDNILLELFTHVPARQLLLNCRLVCSLWRDLIDLLTLWKRKCLRKGFITKDWDQPVADW

       130        140        150        160        170        180
KIFYFLRSLHRNLLRNPCAENDMFAWQIDFNGGDRWKVDSLPGAHGTEFPDPKVKKSFVT

       190        200        210        220        230        240
SYELCLKWELVDLLADRYWEELLDTFRPDIVVKDWFAARADCGCTYQLKVQLASADYFVL

       250        260        270        280        290        300
ASFEPPPVTIQQWNNATWTEVSYTFSDYPRGVRYILFQHGGRDTQYWAGWYGPRVTNSSI

       310        320        330
VVSPKMTRNQASSEAQPGQKHGQEEAAQSPYGAVVQIF
```

FIG.9A

```
        10         20         30         40         50         60         70         80         90
GCGCGTTCGGGAGCTTCGGCCCTGCGTAGGAGGCGGGTGCAGGTGTGGGTGCTGAGCCGCCCGCCGCCTGGAGGGGGAGACAGCTTCAGGACAC

    100        110        120        130        140        150        160        170        180
GCAGGCCGCAGCGAGGGCCCGGGCCCCGGGGGATCCCAGGCCATGGACGCTCCCCACTCCAAAGCAGCCCTGGACAGCATTAACGAGCTGCCCGA

190        200        210        220        230        240        250        260        270        280
TAACATCCTGCTGGAGCTGTTCACGCACGTGCCCGCCCGCCAGCTGCTGCTGAACTGCCGCCTGGTCTGCAGCCTCTGGCGGGACCTCATCGAC

      290        300        310        320        330        340        350        360        370
CTCCTGACCCTCTGGAAACGCAAGTGCCTGCGAAAGGGCTTCATCACCAAGGACTGGGACCAGCCCGTGGCCGACTGGAAAATCTTCTACTTCC

 380        390        400        410        420        430        440        450        460        470
TACGGAGCCTGCATAGGAACCTCCTGCGCAACCCGTGTGCTGAAAACGATATGTTTGCATGGCAAATTGATTTCAATGGTGGGGACCGCTGGAA

        480        490        500        510        520        530        540        550        560
GGTGGATAGCCTCCCTGGAGCCCACGGGACAGAATTTCCTGACCCCAAAGTCAAGAAGTCTTTTGTCACATCCTACGAACTGTGCCTCAAGTGG

    570        580        590        600        610        620        630        640        650
GAGCTGGTGGACCTTCTAGCCGACCGCTACTGGGAGGAGCTACTAGACACATTCCGGCCGGACATCGTGGTTAAGGACTGGTTTGCTGCCAGAG

660        670        680        690        700        710        720        730        740        750
CCGACTGTGGCTGCACCTACCAACTCAAAGTGCAGCTGGCCTCGGCTGACTACTTCGTGTTGGCCTCCTTCGAGCCCCCACCTGTGACCATCCA

      760        770        780        790        800        810        820        830        840
ACAGTGGAACAATGCCACATGGACAGAGGTCTCCTACACCTTCTCAGACTACCCCCGGGGTGTCCGCTACATCCTCTTCCAGCATGGGGGCAGG

 850        860        870        880        890        900        910        920        930        940
GACACCCAGTACTGGGCAGGCTGGTATGGGCCCCGAGTCACCAACAGCAGCATTGTCGTCAGCCCCAAGATGACCAGGAACCAGGCCTCGTCCG
```

FIG.9B

950 960 970 980 990 1000 1010 1020 1030
AGGCTCAGCCTGGGCAGAAGCATGGACAGGAGGAGGCTGCCCAATCGCCCTACGGAGCTGTTGTCCAGATTTTCTGACAGCTGTCCATCCTGTG

1040 1050 1060 1070 1080 1090 1100 1110 1120
TCTGGGTCAGCCAGAGGTTCCTCCAGGCAGGAGCTGAGCATGGGGTGGGCAGTGAGGTCCCTGTACCAGCGACTCCTGCCCCGGTTCAACCCTA

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
CCAGCTTGTGGTAACTTACTGTCACATAGCTCTGACGTTTTGTTGTAATAAATGTTTTCAGGCCGGGCACTGTGGCTCACGCCTGTAATCCCAG

1230 1240 1250 1260 1270 1280 1290 1300 1310
CACTTTGGGAGACCGAGGCAGGTGGATCACGAGGTCAGGAGACAGAGACCATCCTGGCCAACACGGTGAAACCCTGTCTCTACTAAAAATACAA

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
AAAATTAGCCGGGCGTGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGGGAGGCTGATGCAGAAGAATGGCGTGAACCCGGAAGGCAGAGCTTGC

1420 1430 1440 1450 1460 1470 1480 1490 1500
AGTGAGCCGAGATCACGCCACTGCACTCCAGCCTGGGTGACAGAGCGAGACTCTGGCTCATAAAATAATAATAATAATAAATAAATAAAAAATA

1510 1520 1530
AATGGTTTTCAGTAAAAAAAAAAAAAAAAA

FIG.9C

```
        10         20         30         40         50         60
MSNTRFTITLNYKDPLTGDEETLASYGIVSGDLICLILHDDIPPPNIPSSTDSEHSSLQN

        70         80         90        100        110        120
NEQPSLATSSNQTSIQDEQPSDSFQGQAAQSGVWNDDSMLGPSQNFEAESIQDNAHMAEG

       130        140        150        160        170        180
TGFYPSEPLLCSESVEGQVPHSLETLYQSADCSDANDALIVLIHLLMLESGYIPQGTEAK

       190        200        210        220        230        240
ALSLPEKWKLSGVYKLQYMHHLCEGSSATLTCVPLGNLIVVNATLKINNEIRSVKRLQLL

       250        260        270        280        290        300
PESFICKEKLGENVANIYKDLQKLSRLFKDQLVYPLLAFTRQALNLPNVFGLVVLPLELK

       310        320        330        340        350        360
LRIFRLLDVRSVLSLSAVCRDLFTASNDPLLWRFLYLRDFRDNTVRVQDTDWKELYRKRH

       370        380        390        400        410        420
IQRKESPKGRFVLLLPSSTHTIPFYPNPLHPRPFPSSRLPPGIIGGEYDQRPTLPYVGDP

       430        440        450        460        470        480
ISSLIPGPGETPSQLPPLRPRFDPVGPLPGPNPILPGRGGPNDRFPFRPSRGRPTDGRLS

FM
```

FIG.10A

```
        10         20         30         40         50         60         70         80         90
TGGAATTCCCATGGACCATGTCTAATACCCGATTTACAATTACATTGAACTACAAGGATCCCCTCACTGGAGATGAAGAGACCTTGGCTTCATA

   100        110        120        130        140        150        160        170        180
TGGGATTGTTTCTGGGGACTTGATATGTTTGATTCTTCACGATGACATTCCACCGCCTAATATACCTTCATCCACAGATTCAGAGCATTCTTCA

190        200        210        220        230        240        250        260        270        280
CTCCAGAACAATGAGCAACCCTCTTTGGCCACCAGCTCCAATCAGACTAGCATACAGGATGAACAACCAAGTGATTCATTCCAAGGACAGGCAG

     290        300        310        320        330        340        350        360        370
CCCAGTCTGGTGTTTGGAATGACGACAGTATGTTAGGGCCTAGTCAAAATTTTGAAGCTGAGTCAATTCAAGATAATGCGCATATGGCAGAGGG

 380        390        400        410        420        430        440        450        460        470
CACAGGTTTCTATCCCTCAGAACCCCTGCTCTGTAGTGAATCGGTGGAAGGGCAAGTGCCACATTCATTAGAGACCTTGTATCAATCAGCTGAC

       480        490        500        510        520        530        540        550        560
TGTTCTGATGCCAATGATGCGTTGATAGTGTTGATACATCTTCTCATGTTGGAGTCAGGTTACATACCTCAGGGCACCGAAGCCAAAGCACTGT

   570        580        590        600        610        620        630        640        650
CCCTGCCGGAGAAGTGGAAGTTGAGCGGGGTGTATAAGCTGCAGTACATGCATCATCTCTGCGAGGGCAGCTCCGCTACTCTCACCTGTGTGCC

660        670        680        690        700        710        720        730        740        750
TTTGGGAAACCTGATTGTTGTAAATGCTACACTAAAAATCAACAATGAGATTAGAAGTGTGAAAAGATTGCAGCTGCTACCAGAATCTTTTATT

     760        770        780        790        800        810        820        830        840
TGCAAAGAGAAACTAGGGGAAAATGTAGCCAACATATACAAAGATCTTCAGAAACTCTCTCGCCTCTTTAAAGACCAGCTGGTGTATCCTCTTC

 850        860        870        880        890        900        910        920        930        940
TGGCTTTTACCCGACAAGCACTGAACCTACCAAATGTATTTGGGTTGGTCGTCCTCCCATTGGAACTGAAACTACGGATCTTCCGACTTCTGGA
```

FIG.10B

950 960 970 980 990 1000 1010 1020 1030
TGTTCGTTCCGTCTTGTCTTTGTCTGCGGTTTGTCGTGACCTCTTTACTGCTTCAAATGACCCACTCCTGTGGAGGTTTTTATATCTGCGTGAT

1040 1050 1060 1070 1080 1090 1100 1110 1120
TTTCGAGACAATACTGTCAGAGTTCAAGACACAGATTGGAAAGAACTGTACAGGAAGAGGCACATACAAAGAAAAGAATCCCCGAAAGGGCGGT

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
TTGTGCTGCTCCTGCCATCGTCAACCCACACCATTCCATTCTATCCCAACCCCTTGCACCCTAGGCCATTTCCTAGCTCCCGCCTTCCTCCAGG

1230 1240 1250 1260 1270 1280 1290 1300 1310
AATTATCGGGGGTGAATATGACCAAAGACCAACACTTCCCTATGTTGGAGACCCAATCAGTTCACTCATTCCTGGTCCTGGGGAGACGCCCAGC

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
CAGTTACCTCCACTGAGACCACGCTTTGATCCAGTTGGCCCACTTCCAGGACCTAACCCCATCTTGCCAGGGCGAGGCGGCCCCAATGACAGAT

1420 1430 1440 1450 1460 1470 1480 1490 1500
TTCCCTTTAGACCCAGCAGGGGTCGGCCAACTGATGGCCGCCTGTCATTCATGTGATTGATTTGTAATTTCATTTCTGGAGCTCCATTTGTTTT

1510 1520 1530 1540 1550 1560 1570 1580 1590
TGTTTCTAAACTACAGATGTCACTCCTTGGGGTGCTGATCTCGAGTGTTATTTTCTGATTGTGGTGTTGAGAGTTGCACTCCCAGAAACCTTTT

1600 1610 1620 1630 1640 1650 1660 1670 1680 1690
AAGAGATACATTTATAGCCCTAGGGGTGGTATGACCCAAAGGTTCCTCTGTGACAAGGTTGGCCTTGGGAATAGTTGGCTGCCAATCTCCCTGC

1700 1710 1720 1730 1740 1750 1760
TCTTGGTTCTCCTCTAGATTGAAGTTTGTTTTCTGATGCTGTTCTTACCAGATTAAAAAAAAGTGTAAATT

FIG.10C

```
        10         20         30         40         50         60
ETSKLG*SAVLAPAAGGTLSSEGRSAVSGILIAVTSTGVDK*SLNQLLHGLGTSSRLSHF

        70         80         90        100        110        120
PFG*KSPPRGQFVAAAVEIAGRSGLQMGQGLWRVVRNQQLQQEGYSEQGYLTREQSRRMA

       130        140        150        160        170        180
ASNISNTNHRKQVQGGIDIYHLLKARKSKEQEGFINLEMLPPELSFTILSYLNATDLCLA

       190        200        210        220        230        240
SCVWQDLANDELLWQGLCKSTWGHCSIYNKNPPLGFSFRKXYMQLDEGSLTFNANPDEGV

       250        260        270        280        290        300
NYFMSKGILDDSPKEIAKFIFCTRTLNWKKLRIYLDERRDVLDDLVTLHNFRNQFLPNAL

       310        320        330        340        350        360
REFFRHIHAPEERGEYLETLITKFSHRFCACNPDLMRELGLSPDAVYVLCYSLILLSIDL

       370        380        390        400        410        420
TSPHVKNKMSKREFIRNTRRAAQNISEDFVGHLYDNIYLIGHVAA*KAQLLGLQFLLQTK

       430        440        450        460        470        480
ATQGLSRYGGYISAGHCSLSIQSSFSVQPFFLLPFSILVISLGN*IILQNFS*FCLSRFA

       490        500        510        520        530        540
QSRATV*HSC*RMIN*HYTLKDGVFVH*ICLKNFIHFHSLYKYHVMCTYLTKEIYSHNYF

       550        560        570        580        590        600
IVKILTKVFPFLSN*VLKFI*F*SETIVXVKVRSDFRQKPIPASFSFKL*RVLICYYITM

       610        620        630        640        650
QNWQLFL*YKFII*FFILKTGLIKSR*VL*TI*DF*NIKIYDLHS*E*NKIXLELW
```

FIG.11A

```
        10         20         30         40         50         60         70         80         90
GGAAACGTCAAAATTGGGATAGTCGGCAGTTCTGGCCCCTGCAGCTGGAGGTACCCTGAGTTCTGAGGGTCGTAGTGCTGTTTCTGGTATTCTC

    100        110        120        130        140        150        160        170        180
ATCGCGGTCACCTCTACCGGTGTGGACAAGTAAAGTTTGAATCAGCTTCTCCATGGCCTGGGCACCAGTTCCCGGCTGAGCCATTTTCCTTTTG

190        200        210        220        230        240        250        260        270        280
GCTAAAAGTCCCCGCCCAGAGGCCAATTCGTCGCGGCGGCGGTGGAGATCGCAGGTCGCTCAGGCTTGCAGATGGGTCAAGGGTTGTGGAGAGT

     290        300        310        320        330        340        350        360        370
GGTCAGAAACCAGCAGCTGCAACAAGAAGGCTACAGTGAGCAAGGCTACCTCACCAGAGAGCAGAGCAGGAGAATGGCTGCGAGCAACATTTCT

 380        390        400        410        420        430        440        450        460        470
AACACCAATCATCGTAAACAAGTCCAAGGAGGCATTGACATATATCATCTTTTGAAGGCAAGGAAATCGAAAGAACAGGAAGGATTCATTAATT

        480        490        500        510        520        530        540        550        560
TGGAAATGTTGCCTCCTGAGCTAAGCTTTACCATCTTGTCCTACCTGAATGCAACTGACCTTTGCTTGGCTTCATGTGTTTGGCAGGACCTTGC

    570        580        590        600        610        620        630        640        650
GAATGATGAACTTCTCTGGCAAGGGTTGTGCAAATCCACTTGGGGTCACTGTTCCATATACAATAAGAACCCACCTTTAGGATTTTCTTTTAGA

660        670        680        690        700        710        720        730        740        750
AAAKTGTATATGCAGCTGGATGAAGGCAGCCTCACCTTTAATGCCAACCCAGATGAGGGAGTGAACTACTTTATGTCCAAGGGTATCCTGGATG

     760        770        780        790        800        810        820        830        840
ATTCGCCAAAGGAAATAGCAAAGTTTATCTTCTGTACAAGAACACTAAATTGGAAAAAACTGAGAATCTATCTTGATGAAAGGAGAGATGTCTT

 850        860        870        880        890        900        910        920        930        940
GGATGACCTTGTAACATTGCATAATTTTAGAAATCAGTTCTTGCCAAATGCACTGAGAGAATTTTTTCGTCATATCCATGCCCCTGAAGAGCGT
```

FIG.11B

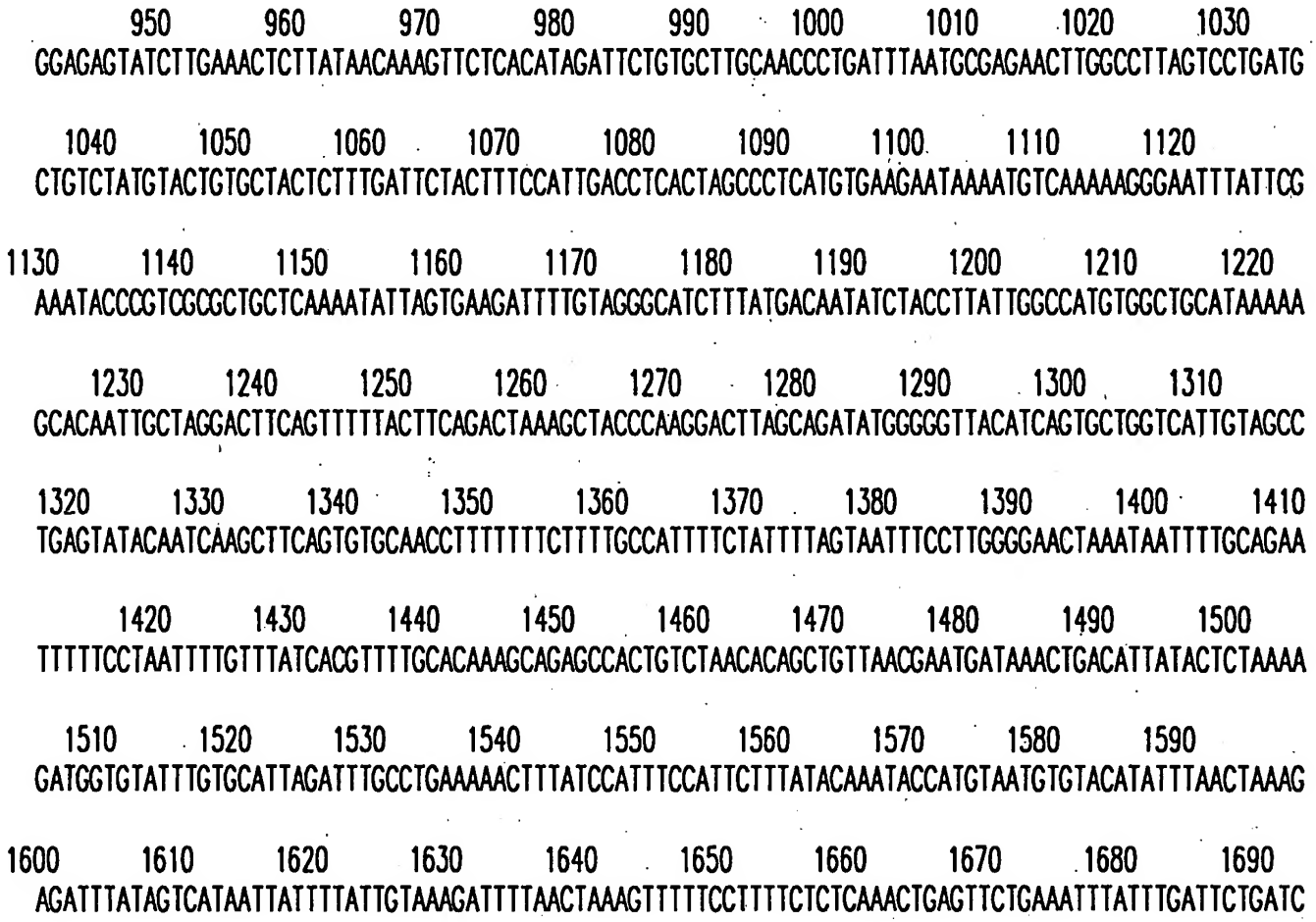

950 960 970 980 990 1000 1010 1020 1030
GGAGAGTATCTTGAAACTCTTATAACAAAGTTCTCACATAGATTCTGTGCTTGCAACCCTGATTTAATGCGAGAACTTGGCCTTAGTCCTGATG
1040 1050 1060 1070 1080 1090 1100 1110 1120
CTGTCTATGTACTGTGCTACTCTTTGATTCTACTTTCCATTGACCTCACTAGCCCTCATGTGAAGAATAAAATGTCAAAAAGGGAATTTATTCG
1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
AAATACCCGTCGCGCTGCTCAAAATATTAGTGAAGATTTTGTAGGGCATCTTTATGACAATATCTACCTTATTGGCCATGTGGCTGCATAAAAA
1230 1240 1250 1260 1270 1280 1290 1300 1310
GCACAATTGCTAGGACTTCAGTTTTTACTTCAGACTAAAGCTACCCAAGGACTTAGCAGATATGGGGGTTACATCAGTGCTGGTCATTGTAGCC
1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
TGAGTATACAATCAAGCTTCAGTGTGCAACCTTTTTTTCTTTTGCCATTTTCTATTTTAGTAATTTCCTTGGGGAACTAAATAATTTTGCAGAA
1420 1430 1440 1450 1460 1470 1480 1490 1500
TTTTTCCTAATTTTGTTTATCACGTTTTGCACAAAGCAGAGCCACTGTCTAACACAGCTGTTAACGAATGATAAACTGACATTATACTCTAAAA
1510 1520 1530 1540 1550 1560 1570 1580 1590
GATGGTGTATTTGTGCATTAGATTTGCCTGAAAAACTTTATCCATTTCCATTCTTTATACAAATACCATGTAATGTGTACATATTTAACTAAAG
1600 1610 1620 1630 1640 1650 1660 1670 1680 1690
AGATTTATAGTCATAATTATTTTATTGTAAAGATTTTAACTAAAGTTTTTCCTTTTCTCTCAAACTGAGTTCTGAAATTTATTTGATTCTGATC

FIG.11C

1700 1710 1720 1730 1740 1750 1760 1770 1780
TGAAACTATTGTCTYCGTAAAAGTTAGATCTGACTTCAGRCAGAAACCAATACCAGCTTCCTTTTCCTTTAAACTTTGAAGAGTGTTGATTTGT

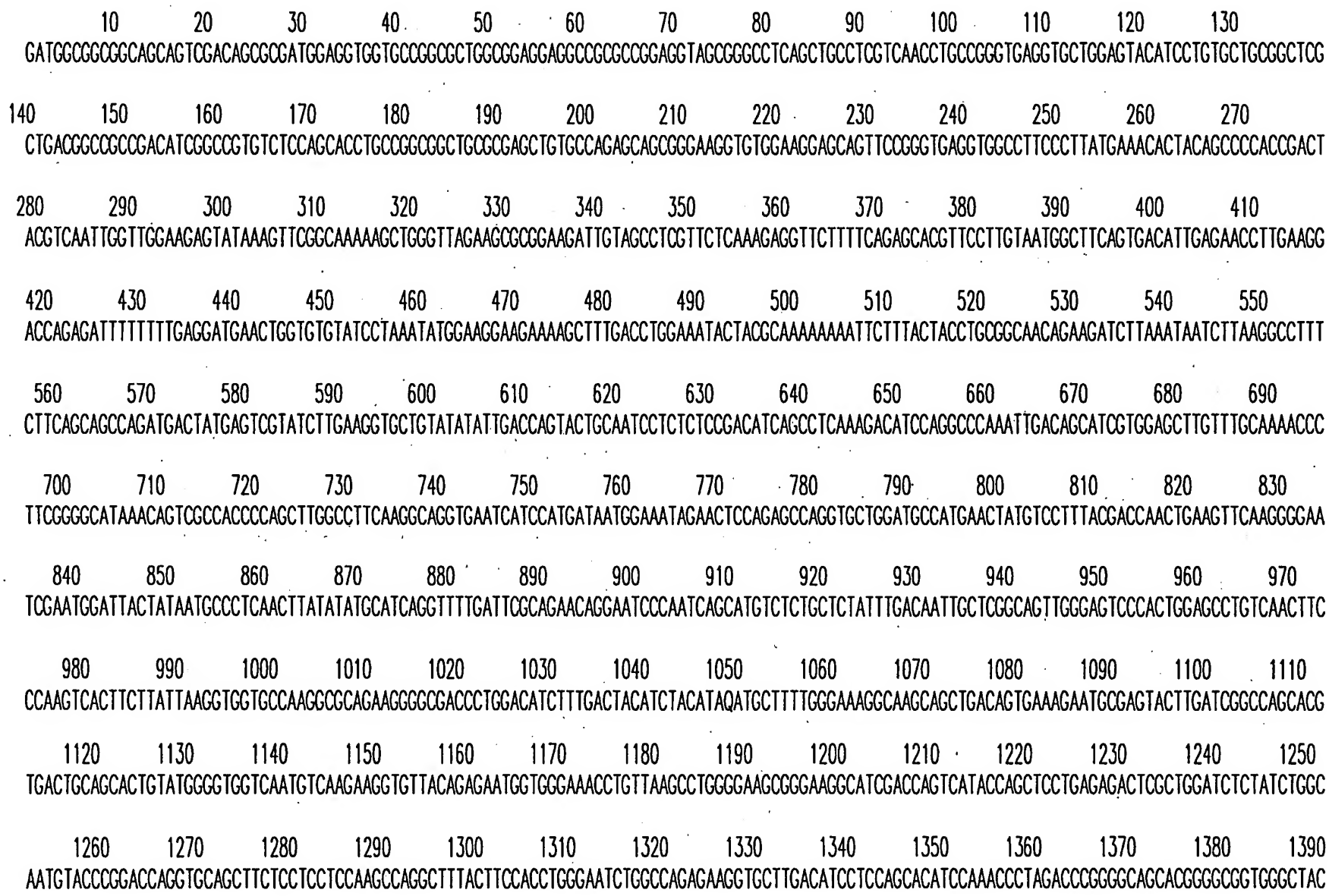
1790 1800 1810 1820 1830 1840 1850 1860 1870 1880
TACTATATTACTATGCAAAACTGGCAGTTATTTTTATAATATAAATTTATAATTTGATTTTTTATTTTAAAAACTGGGTTAATCAAGTCTCGGT

1890 1900 1910 1920 1930 1940 1950 1960 1970
AAGTCCTTTAAACCATTTAGGATTTTTAAAACATCAAAATTTATGATTTACATTCATAGGAATAAAATAAAATATYATTAGAACTCTGGT

FIG.11D

```
        10         20         30         40         50         60
MAAAAVDSAMEVVPALAEEAAPEVAGLSCLVNLPGEVLEYILCCGSLTAADIGRVSSTCR

        70         80         90        100        110        120

RLRELCQSSGKVWKEQFRVRWPSLMKHYSPTDYVNWLEEYKVRQKAGLEARKIVASFSKR

       130        140        150        160        170        180

FFSEHVPCNGFSDIENLEGPEIFFEDELVCILNMEGRKALTWKYYAKKILYYLRQQKILN

       190        200        210        220        230        240
NLKAFLQQPDDYESYLEGAVYIDQYCNPLSDISLKDIQAQIDSIVELVCKTLRGINSRHP

       250        260        270        280        290        300
SLAFKAGESSMIMEIELQSQVLDAMNYVLYDQLKFKGNRMDYYNALNLYMHQVLIRRTGI

       310        320        330        340        350        360
PISMSLLYLTIARQLGVPLEPVNFPSHFLLRWCQGAEGATLDIFDYIYIDAFGKGKQLTV

       370        380        390        400        410        420
KECEYLIGQHVTAALYGVVNVKKVLQRMVGNLLSLGKREGIDQSYQLLRDSLDLYLAMYP

       430        440        450        460        470        480
DQVQLLLLQARLYFHLGIWPEKVLDILQHIQTLDPGQHGAVGYLVQHTLEHIERKKEEVG

       490        500        510        520        530        540
VEVKLRSDEKHRDVCYSIGLIMKHKRYGYNCVIYGWDPTCMMGHEWIRNMNVHSLPHGHH

       550        560        570        580        590        600
QPFYNVLVEDGSCRYAAQENLEYNVEPQEISHPDVGRYFSEFTGTHYIPNAELEIRYPED

       610        620
LEFVYETVQNIYSAKKENIDE
```

FIG.12A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140 150 160 170 180 190 200 210 220 230 240 250 260 270
CTGACGGCCGCCGACATCGGCCGTGTCTCCAGCACCTGCCGGCGGCTGCGCGAGCTGTGCCAGAGCAGCGGGAAGGTGTGGAAGGAGCAGTTCCGGGTGAGGTGGCCTTCCCTTATGAAACACTACAGCCCCACCGACT
280 290 300 310 320 330 340 350 360 370 380 390 400 410
ACGTCAATTGGTTGGAAGAGTATAAAGTTCGGCAAAAAGCTGGGTTAGAAGCGCGGAAGATTGTAGCCTCGTTCTCAAAGAGGTTCTTTTCAGAGCACGTTCCTTGTAATGGCTTCAGTGACATTGAGAACCTTGAAGG
420 430 440 450 460 470 480 490 500 510 520 530 540 550
ACCAGAGATTTTTTTTGAGGATGAACTGGTGTGTATCCTAAATATGGAAGGAAGAAAAGCTTTGACCTGGAAATACTACGCAAAAAAAATTCTTTACTACCTGCGGCAACAGAAGATCTTAAATAATCTTAAGGCCTTT
560 570 580 590 600 610 620 630 640 650 660 670 680 690
CTTCAGCAGCCAGATGACTATGAGTCGTATCTTGAAGGTGCTGTATATATTGACCAGTACTGCAATCCTCTCTCCGACATCAGCCTCAAAGACATCCAGGCCCAAATTGACAGCATCGTGGAGCTTGTTTGCAAAACCC
700 710 720 730 740 750 760 770 780 790 800 810 820 830
TTCGGGGCATAAACAGTCGCCACCCCAGCTTGGCCTTCAAGGCAGGTGAATCATCCATGATAATGGAAATAGAACTCCAGAGCCAGGTGCTGGATGCCATGAACTATGTCCTTTACGACCAACTGAAGTTCAAGGGGAA
840 850 860 870 880 890 900 910 920 930 940 950 960 970
TCGAATGGATTACTATAATGCCCTCAACTTATATATGCATCAGGTTTTGATTCGCAGAACAGGAATCCCAATCAGCATGTCTCTGCTCTATTTGACAATTGCTCGGCAGTTGGGAGTCCCACTGGAGCCTGTCAACTTC
980 990 1000 1010 1020 1030 1040 1050 1060 1070 1080 1090 1100 1110
CCAAGTCACTTCTTATTAAGGTGGTGCCAAGGCCCAGAAGGGCCGACCCTGGACATCTTTGACTACATCTACATAQATGCTTTTGGGAAAGGCAAGCAGCTGACAGTGAAAGAATGCGAGTACTTGATCGGCCAGCACG
1120 1130 1140 1150 1160 1170 1180 1190 1200 1210 1220 1230 1240 1250
TGACTGCAGCACTGTATGGGGTGGTCAATGTCAAGAAGGTGTTACAGAGAATGGTGGGAAACCTGTTAAGCCTGGGGAAGCGGGAAGGCATCGACCAGTCATACCAGCTCCTGAGAGACTCGCTGGATCTCTATCTGGC
1260 1270 1280 1290 1300 1310 1320 1330 1340 1350 1360 1370 1380 1390
AATGTACCCGGACCAGGTGCAGCTTCTCCTCCTCCAAGCCAGGCTTTACTTCCACCTGGGAATCTGGCCAGAGAAGGTGCTTGACATCCTCCAGCACATCCAAACCCTAGACCCGGGGCAGCACGGGGCGGTGGGCTAC

FIG.12B

1400 1410 1420 1430 1440 1450 1460 1470 1480 1490 1500 1510 1520
CTGGTGCAGCACACTCTAGAGCACATTGAGCGCAAAAAGGAGGAGGTGGGCGTAGAGGTGAAGCTGCGCTCCGATGAGAAGCACAGAGATGTCTGCTACTCCATCGGGCTCATTATGAAGCATAAGAGGTATGGCTATA

1530 1540 1550 1560 1570 1580 1590 1600 1610 1620 1630 1640 1650 1660
ACTGTGTGATCTACGGCTGGGACCCCACCTGCATGATGGGACACGAGTGGATCCGGAACATGAACGTCCACAGCCTGCCGCACGGCCACCACCAGCCTTTCTATAACGTGCTGGTGGAGGACGGCTCCTGTCGATACGC

1670 1680 1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
AGCCCAAGAAAACTTGGAATATAACGTGGAGCCTCAAGAAATCTCACACCCTGACGTGGGACGCTATTTCTCAGAGTTTACTGGCACTCACTACATCCCAAACGCAGAGCTGGAGATCCGGTATCCAGAAGATCTGGAG

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920 1930 1940
TTTGTCTATGAAACGGTGCAGAATATTTACAGTGCAAAGAAAGAGAACATAGATGAGTAAAGTCTAGAGAGGACATTGCACCTTTGCTGCTGCTGCTATCTTCCAAGAGAACGGGACTCCGGAAGAAGACGTCTCCACG

1950 1960 1970 1980 1990 2000 2010 2020 2030 2040 2050 2060 2070 2080
GAGCCCTCGGGACCTGCTGCACCAGGAAAGCCACTCCACCAGTAGTGCTGGTTGCCTCCTACTAAGTTTAAATACCGTGTGCTCTTCCCCAGCTGCAAAGACAATGTTGCTCTCCGCCTACACTAGTGAATTAATCTGA

2090 2100 2110 2120 2130 2140 2150 2160 2170 2180 2190 2200 2210 2220
AAGGCACTGTGTCAGTGGCATGGCTTGTATGCTTGTCCTGTGGTGACAGTTTGTGACATTCTGTCTTCATGAGGTCTCACAGTCGACGCTCCTGTAATCATTCTTTGTATTCACTCCATTCCCCTGTCTGTCTGCATTT

2230 2240 2250 2260 2270 2280 2290 2300 2310 2320 2330 2340 2350 2360
GTCTCAGAACATTTCCTTGGCTGGACAGATGGGGTTATGCATTTGCAATAATTTCCTTCTGATTTCTCTGTGGAACGTGTTCGGTCCCGAGTGAGGACTGTGTGTCTTTTTACCCTGAAGTTAGTTGCATATTCAGAGG

2370 2380 2390 2400 2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
TAAAGTTGTGTGCTATCTTGGCAGCATCTTAGAGATGGAGACATTAACAAGCTAATGGTAATTAGAATCATTTGAATTTATTTTTTTCTAATATGTGAAACACAGATTTCAAGTGTTTTATCTTTTTTTTTTAAATTTA

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600 2610 2620 2630 2640
AATGGGAATATAACACAGTTTTCCCTTCCATATTCCTCTCTTGAGTTTATGCACATCTCTATAAATCATTAGTTTTCTATTTTATTACATAAAATTCTTTTAGAAAATGCAAATAGTGAACTTTGTGAATGGATTTTTC

2650 2660 2670 2680 2690 2700 2710 2720 2730 2740 2750 2760 2770 2780
CATACTCATCTACAATTCCTCCATTTTAAATGACTACTTTTATTTTTTAATTTAAAAAATCTACTTCAGTATCATGAGTAGGTCTTACATCAGTGATGGGTTCTTTTTGTAGTGAGACATACAAATCTGATGTTAATGT

FIG.12C

2790 2800 2810 2820 2830 2840 2850 2860 2870 2880 2890 2900 2910
TTGCTCTTAGAAGTCATACTCCATGGTCTTCAAAGACCAAAAAATGAGGTTTTGCCTTTGTAATCAGGAAAAAAAAAAATTAATGAACCTTAAAAAAAAAAAAAAAAGGTTTTGAAGGGAAAAAAAGTGGTTTCACACCT

2920 2930 2940 2950 2960 2970 2980 2990 3000 3010 3020 3030 3040 3050
CTTGTTATTCCTTAGAGTCACTTCAAGGCCTGTTTGAATGTGGCAGGTTAGAAAGAGAGAGAATGTCTTTCATTTGAAGAGTGTTGGACTTGTGTGAAAGGAGATGTGCGTGTTGGAATCTGCTTTTCCAAGCCGCCAG

3060 3070 3080 3090 3100 3110 3120 3130 3140 3150 3160 3170 3180 3190
GGTCCTGACGGCAGCAGGACGAAGCCTGTTGTGGCGTCTTCTGGGAAAGCCTGACCGTGTGTTCGGACGGCACTGGCTCCTTTCCGAAGTTCTCAGTAACTGAGCCCAGAGTAACTGCACGCCTTTGTGCAGCTCTGGA

3200 3210 3220 3230 3240 3250 3260 3270 3280 3290 3300 3310 3320 3330
GCTCCACCAACTCTCGGCCTGCCAGTTCTCAAGCGAGCTAATCTTGTCATTAATCGATAGAAGCTAACTTCCGAAGTTAGGACCTAGTTACTTTGCTCTCAACATTTAAAATAATGCAGTTGCTCTAGTGAATGGGGCG

3340 3350 3360 3370 3380 3390 3400 3410 3420 3430 3440 3450 3460 3470
TTAGGGGCCTGTCTCTGCACCTGTCTGTCCATCTGCATGCAGTATTCTCACCCATGTTGAATGCCTGCTGCTTGTTTACCCTTTGGAAACCCTGGGGTGACCAAGGTTTGGAAAGCCACCTGAGACCACTTCATAGCAA

3480 3490 3500 3510 3520 3530 3540 3550 3560 3570 3580 3590 3600 3610
GGGAAGGCTTTAAGCAGTTACTAGAAAGAGATGGGGATTTGGCCCCTGGCTCCTCCAGCCTGAATGAGCTATTTAATCCACTGTCCATGTTCCTCATCAGTCAAATCCAAAGTCAAAGGATTTGAACCTGCATCTGGAA

3620 3630 3640 3650 3660 3670 3680 3690 3700 3710 3720 3730 3740 3750
ACGTAACCACTCACAGCACCTGGCCCGCCAAGGTTGGGAGGATTGTACACTACTTTCATTTAAAGGGGAAAGTTTGATAATACGGAATTAATTAATATGAATGAGATGCATTAATAAGAACCTGAGCATGCTGAGAGTT

3760 3770 3780 3790 3800 3810 3820 3830 3840 3850 3860 3870 3880 3890
GCAATTGTTGGTTTTCTGGTTTGATTGATTTCCTTTTTTCTTAGACACATCAAAGTCAAGAAAGATGGTTTTACCTTTACTGACCCAGCTGTACATATGTATCTAGACTGTTTTTAAATGTCTTTCTTCATGAATGCTT

3900 3910 3920 3930 3940 3950 3960 3970 3980 3990 4000 4010 4020 4030
CATGGGGCTCCAGGAAGCCTGTATCACCTGTGTAAGTTGGTATTTGGGCACTTTATATTTTTCTAAAAACGTGTTTTGGATCCTGTACTCTAATAAATCATAAGTTTCTTTTTAAAAATTTTCCAAAACTTTTCTCCAT

4040 4050 4060 4070 4080 4090 4100 4110 4120 4130 4140 4150 4160
TTTAAAAAGCCCTGTTATAAACGTTGAACTTTCACAATGTTAAAATGTTAAATATTTGGATATAGCAACTTCTTTTCTCTTCAAATGAATGCCAAGATTTTTTTGTACAATGATTAATAAATGGAACTTATCCAGAG

FIG.12D

```
        10         20         30         40         50         60

RSTGFRRAGEEWSR*XLAASPGXLRRPAXTFVLSNLAEVVERVLTFLPAKALLRVACVCR

        70         80         90
LWRECVRRVLRTHRSVTWISAGLAEAGHLXGH
```

FIG.13A

```
        10         20         30         40         50         60
CCGTAGTACTGGNTTCCGGCGGGCTGGTGAGGAATGGAGCCGGTAGNTGCTTGCGGCGAG

        70         80         90        100        110        120
TCCCGGGNTCCTCCGTAGACCCGCGGANACCTTCGTGTTGAGTAACCTGGCGGAGGTGGT

       130        140        150        160        170        180
GGAGCGTGTGCTCACCTTCCTGCCCGCCAAGGCGTTGCTGCGGGTGGCCTGCGTGTGCCG

       190        200        210        220        230        240
CTTATGGAGGGAGTGTGTGCGCAGAGTATTGCGGACCCATCGGAGCGTAACCTGGATCTC

       250        260        270
CGCAGGCCTGGCGGAGGCCGGCCACCTGGNGGGGCATT
```

FIG.13B

```
        10         20         30         40         50         60
RPRPVQQQQQQPPQQPPPQPPQQQPPQQQPPPPPQQQQQQQPPPPPPPPPPLPQERNNVG

        70         80         90        100        110        120
ERDDDVPADMVAEESGPGAQNSPYQLRRKTLLPKRTACPTKNSMEGASTSTTENFGHRAK

       130        140        150        160        170        180

RARVSGKSQDLSAAPAEQYLQEKLPDEVVLKIFSYLLEQDLCRAACVCKRFSELANDPNL

       190
WKRLYMEVFEYTRPMMH
```

FIG.14A

```
        10         20         30         40         50         60

GCGGCCGCGCCCGGTGCAGCAACAGCAGCAGCAGCCCCCGCAGCAGCCGCCGCCGCAGCC

        70         80         90        100        110        120
GCCCCAGCAGCAGCCGCCCCAGCAGCAGCCTCCGCCGCCGCCGCAGCAGCAGCAGCAGCA

       130        140        150        160        170        180
GCAGCCTCCGCCGCCGCCACCGCCGCCTCCGCCGCTGCCTCAGGAGCGGAACAACGTCGG

       190        200        210        220        230        240
CGAGCGGGATGATGATGTGCCTGCAGATATGGTTGCAGAAGAATCAGGTCCTGGTGCACA

       250        260        270        280        290        300
AAATAGTCCATACCAACTTCGTAGAAAAACTCTTTTGCCGAAAAGAACAGCGTGTCCCAC

       310        320        330        340        350        360
AAAGAACAGTATGGAGGGCGCCTCAACTTCAACTACAGAAAACTTTGGTCATCGTGCAAA

       370        380        390        400        410        420
ACGTGCAAGAGTGTCTGGAAAATCACAAGATCTATCAGCAGCACCTGCTGAACAGTATCT

       430        440        450        460        470        480
TCAGGAGAAACTGCCAGATGAAGTGGTTCTAAAAATCTTCTCTTACTTGCTGGAACAGGA

       490        500        510        520        530        540
TCTTTGTAGAGCAGCTTGTGTATGTAAACGCTTCAGTGAACTTGCTAATGATCCCAATTT

       550        560        570        580        590
GTGGAAACGATTATATATGGAAGTATTTGAATATACTCGCCCTATGATGCAT
```

FIG.14B

```
        10         20         30         40         50         60
RPRPGLRGGRAPCEVTMEAGGLPLELWRMILAYLHLPDLGRCSLVCRAWYELILSLDSTR

        70         80         90        100        110        120
WRQLCLGCTECRHPNWPNQPDVEPESWREAFKQHYLASKTWTKNALDLESSICFSLFRRR

       130        140        150        160        170
RERRTLSVGPGREFDSLGSALAMASLYDRIVLFPGVYEEQGEIILKVPVEIVGQGKLG
```

FIG.15A

```
        10         20         30         40         50         60
GCGGCCGCGGCCCGGACTCCGCGGTGGGCGAGCGCCCTGTGAGGTGACCATGGAGGCTGG

        70         80         90        100        110        120
TGGCCTCCCCTTGGAGCTGTGGCGCATGATCTTAGCCTACTTGCACCTTCCCGACCTGGG

       130        140        150        160        170        180
CCGCTGCAGCCTGGTATGCAGGGCCTGGTATGAACTGATCCTCAGTCTCGACAGCACCCG

       190        200        210        220        230        240
CTGGCGGCAGCTGTGTCTGGGTTGCACCGAGTGCCGCCATCCCAATTGGCCCAACCAGCC

       250        260        270        280        290        300
AGATGTGGAGCCTGAGTCTTGGAGAGAAGCCTTCAAGCAGCATTACCTTGCATCCAAGAC

       310        320        330        340        350        360
ATGGACCAAGAATGCCTTGGACTTGGAGTCTTCCATCTGCTTTTCTCTATTCCGCCGGAG

       370        380        390        400        410        420
GAGGGAACGACGTACCCTGAGTGTTGGGCCAGGCCGTGAGTTTGACAGCCTGGGCAGTGC

       430        440        450        460        470        480
CTTGGCCATGGCCAGCCTGTATGACCGAATTGTGCTCTTCCCAGGTGTGTACGAAGAGCA

       490        500        510        520        530
AGGTGAAATCATCTTGAAGGTGCCTGTGGAGATTGTAGGGCAGGGGAAGTTGGGTGA
```

FIG.15B

```
        10         20         30         40         50         60
ETETAPLTLESLPTDPLLLILSFLDYRDLINCCYVSRRLSQLSSHDPLWRRHCKKYWLIS

        70         80         90        100        110        120
EEEKTQKNQCWKSLFIDTYSDVGRYIDHYAAIKKASGMISRNIWSPGVLGWVLSLKEGCS

       130        140        150        160        170        180
RGRPRCCGSADWAASFLDDYRCSYRIHNGQKLVGSWGYWEAWHCLITIVLKIC*TSIQLP

       190        200        210        220        230        240
EIPAETGTEILSPFNFCIHTGLSQYIAVEAAEG*NKNEVFYQCQTVERVFKYGIKMCSDG

       250
CINGMH*VFS
```

FIG.16A

```
        10         20         30         40         50         60
GAGACCGAGACGGCGCCGCTGACCCTAGAGTCGCTGCCCACCGATCCCCTGCTCCTCATC

        70         80         90        100        110        120
TTATCCTTTTTGGACTATCGGGATCTAATCAACTGTTGTTATGTCAGTCGAAGATTAAGC

       130        140        150        160        170        180
CAGCTATCAAGTCATGATCCGCTGTGGAGAAGACATTGCAAAAAATACTGGCTGATATCT

       190        200        210        220        230        240
GAGGAAGAGAAAACACAGAAGAATCAGTGTTGGAAATCTCTCTTCATAGATACTTACTCT

       250        260        270        280        290        300
GATGTAGGAAGATACATTGACCATTATGCTGCTATTAAAAAGGCCTCGGGAATGATCTCA

       310        320        330        340        350        360
AGAAATATTTGGAGCCCAGGTGTCCTCGGATGGGTTTTATCTCTGAAAGAGGGGTGCTCG

       370        380        390        400        410        420
AGAGGAAGACCTCGATGCTGTGGAAGCGCAGATTGGGCTGCAAGTTTCCTGGACGATTAT

       430        440        450        460        470        480
CGATGTTCATACCGAATTCACAATGGACAGAAGTTAGTTGGTTCCTGGGGTTATTGGGAA

       490        500        510        520        530        540
GCATGGCACTGTCTAATCACTATCGTTCTGAAGATTTGTTAGACGTCGATACAGCTGCCG

       550        560        570        580        590        600
GAGATTCCAGCAGAGACAGGGACTGAAATACTGTCTCCCTTTAACTTTTGCATACATACT

       610        620        630        640        650        660
GGTTTGAGTCAGTACATAGCAGTGGAAGCTGCAGAGGGTTGAAACAAAAATGAAGTTTTC

       670        680        690        700        710        720
TACCAATGTCAGACAGTAGAACGTGTGTTTAAATATGGCATTAAGATGTGTTCTGATGGT

       730        740        750
TGTATAAATGGCATGCATTAGGTATTTTCAG
```

FIG.16B

```
        10         20         30         40         50         60
GSGFRAGGWPLTMPGKHQHFQEPEVGCCGKYFLFGFNIVFWVLGALFLAIGLWAWGEKGV

        70         80         90        100        110        120
LSNISALTDLGGLDPVWLVCGSWRRHVGAGLCWAAIGALRENTFLLKFFXXFLGLIFFLE

LA
```

FIG.17A

```
        10         20         30         40         50         60
GGCTCCGGTTTCCGGGCCGGCGGGTGGCCGCTCACCATGCCCGGNAAGCACCAGCATTTC

        70         80         90        100        110        120
CAGGAACCTGAGGTCGGCTGCTGCGGGAAATACTTCCTGTTTGGCTTCAACATTGTCTTC

       130        140        150        160        170        180
TGGGTGCTGGGAGCCCTGTTCCTGGCTATCGGCCTCTGGGCCTGGGGTGAGAAGGGCGTT

       190        200        210        220        230        240
CTCTCGAACATCTCAGCGCTGACAGATCTGGGAGGCCTTGACCCCGTGTGGCTTGTTTGT

       250        260        270        280        290        300
GGTAGTTGGAGGCGTCATGTCGGTGCTGGGCTTTGCTGGGCTGCAATTGGGGCCCTCCGG

       310        320        330        340        350        360
GAGAACACCTTCCTGCTCAAGTTTTTCTNCGNGTTCCTCGGTCTCATCTTCTTCCTGGAG

CTGGCAAC
```

FIG.17B

```
        10         20         30         40         50         60
AAAAAAYLDELPEPLLLRVLAALPAAELVQACRLVCLRWKELVDGAPLWLLKCQQEGLVP

        70         80         90        100        110        120
EGGVEEERDHWQQFYFLSKRRRNLLRNPCGEEDLEGWCDVEHGGDGWRVEELPGDSGVEF

       130        140        150        160        170        180
THDESVKKYFASSFEWCRKAQVIDLQAEGYWEELLDTTQPAIVVKDWYSGRSDAGCLYEL

       190        200        210        220        230        240
TVKLLSEHENVLAEFSSGQVAVPQDSDGGGWMEISHTFTDYGPGVRFVRFEHGGQGSVYW

       250
KGWFGARVTNSSVWVEP*
```

FIG.18A

```
          10         20         30         40         50         60
GCGGCGGCCGCCGCCGCGTACCTGGACGAGCTGCCCGAGCCGCTGCTGCTGCGCGTGCTGGCCGCACTG
70         80         90        100        110        120        130
CCGGCCGCCGAGCTGGTGCAGGCCTGCCGCCTGGTGTGCCTGCGCTGGAAGGAGCTGGTGGACGGCGCC
140        150        160        170        180        190        200
CCGCTGTGGCTGCTCAAGTGCCAGCAGGAGGGGCTGGTGCCCGAGGGCGGCGTGGAGGAGGAGCGCGAC
 210        220        230        240        250        260        270
CACTGGCAGCAGTTCTACTTCCTGAGCAAGCGGCGCCGCAACCTTCTGCGTAACCCGTGTGGGGAAGAG
  280        290        300        310        320        330        340
GACTTGGAAGGCTGGTGTGACGTGGAGCATGGTGGGGACGGCTGGAGGGTGGAGGAGCTGCCTGGAGAC
   350        360        370        380        390        400        410
AGTGGGGTGGAGTTCACCCACGATGAGAGCGTCAAGAAGTACTTCGCCTCCTCCTTTGAGTGGTGTCGC
    420        430        440        450        460        470        480
AAAGCACAGGTCATTGACCTGCAGGCTGAGGGCTACTGGGAGGAGCTGCTGGACACGACTCAGCCGGCC
     490        500        510        520        530        540        550
ATCGTGGTGAAGGACTGGTACTCGGGCCGCAGCGACGCTGGTTGCCTCTACGAGCTCACCGTTAAGCTA
      560        570        580        590        600        610        620
CTGTCCGAGCACGAGAACGTGCTGGCTGAGTTCAGCAGCGGGCAGGTGGCAGTGCCCCAAGACAGTGAC
       630        640        650        660        670        680        690
GGCGGGGGCTGGATGGAGATCTCCCACACCTTCACCGACTACGGGCCGGGCGTCCGCTTCGTCCGCTTC
        700        710        720        730        740        750
GAGCACGGGGGCAGGGCTCCGTCTACTGGAAGGGCTGGTTCGGGGCCCGGGTGACCAACAGCAGCGTG
760        770
TGGGTAGAACCCTGA
```

FIG.18B

```
        10         20         30         40         50         60
MGEKAVPLLRRRRVKRSCPSCGSELGVEEKRGKGNPISIQLFPPELVEHIISFLPVRDLV

        70         80         90        100        110        120
ALGQTCRYFHEVCDGEGVWRRICRRLSPRLQDQDTKGLYFQAFGGRRRCLSKSVAPLLAH

       130        140        150        160        170        180
GYRRFLPTKDHVFILDYVGTLFFLKNALVSTLGQMQWKRACRYVVLCRGAKDFASDPRCD

       190        200        210        220        230        240
TVYRKYLYVLATREPQEVVGTTSSRACDCVEVYLQSSGQRVFKMTFHHSMTFKQIVLVGQ

       250        260        270        280        290        300
ETQRALLLLTEEGKIYSLVVNETQLDQPRSYTVQLALRKVSHYLPHLRVACMTSNQSSTL

       310
YVTDPILCSWLQPPWPGG
```

FIG.19A

```
          10         20         30         40         50         60
ATGGGCGAGAAGGCGGTCCCTTTGCTAAGGAGGAGGCGGGTGAAGAGAAGCTGCCCTTCTTGTGGCTCG

 70        80         90        100        110        120        130
GAGCTTGGGGTTGAAGAGAAGAGGGGGAAAGGAAATCCGATTTCCATCCAGTTGTTCCCCCCAGAGCTG

140        150        160        170        180        190        200
GTGGAGCATATCATCTCATTCCTCCCAGTCAGAGACCTTGTTGCCCTCGGCCAGACCTGCCGCTACTTC

 210        220        230        240        250        260        270
CACGAAGTGTGCGATGGGGAAGGCGTGTGGAGACGCATCTGTCGCAGACTCAGTCCGCGCCTCCAAGAT

 280        290        300        310        320        330        340
CAGGACACGAAGGGCCTGTATTTCCAGGCATTTGGAGGCCGCCGCCGATGTCTCAGCAAGAGCGTGGCC

 350        360        370        380        390        400        410
CCCTTGCTAGCCCACGGCTACCGCCGCTTCTTGCCCACCAAGGATCACGTCTTCATTCTTGACTACGTG

 420        430        440        450        460        470        480
GGGACCCTCTTCTTCCTCAAAAATGCCCTGGTCTCCACCCTCGGCCAGATGCAGTGGAAGCGGGCCTGT

 490        500        510        520        530        540        550
CGCTATGTTGTGTTGTGTCGTGGAGCCAAGGATTTTGCCTCGGACCCAAGGTGTGACACAGTTTACCGT

 560        570        580        590        600        610        620
AAATACCTCTACGTCTTGGCCACTCGGGAGCCGCAGGAAGTGGTGGGTACCACCAGCAGCCGGGCCTGT

 630        640        650        660        670        680        690
GACTGTGTTGAGGTCTATCTGCAGTCTAGTGGGCAGCGGGTCTTCAAGATGACATTCCACCACTCAATG

 700        710        720        730        740        750
ACCTTCAAGCAGATCGTGCTGGTTGGTCAGGAGACCCAGCGGGCTCTACTGCTCCTCACAGAGGAAGGA

760        770        780        790        800        810        820
AAGATCTACTCTTTGGTAGTGAATGAGACCCAGCTTGACCAGCCACGCTCCTACACGGTTCAGCTGGCC

830        840        850        860        870        880        890
CTGAGGAAGGTGTCCCACTACCTGCCTCACCTGCGCGTGGCCTGCATGACTTCCAACCAGAGCAGCACC

 900        910        920        930        940        950
CTCTACGTCACAGATCCTATTCTGTGCTCTTGGCTACAACCACCTTGGCCTGGTGGATGA
```

FIG.19B

```
        10         20         30         40         50         60
RGGSEGRGRGREKRARGARRKRKQGGREARAADGEGGSGPGAEAGARTRPREEAEGGGSV

        70         80         90        100        110        120
EEGARGIIKGDEGSVGAGKEAQGRKYGKEEWRVRARRREGARPGRVQGQGGQVWAYIPGT

       130        140        150        160        170        180
GAAMAAAAREEEEEAARESAACPAAGPALWRLPEVLLLHMCSYLDMRALGRLAQVYRWLW

       190        200        210        220        230        240
HFTNCDLLRRQIAWASLNSGFTRLGTNLMTSVPVKVSQNWIVGCCREGILLKWRCSQMPW

       250        260        270        280        290        300
MQLEDDALYISQANFILAYQFRPDGASLNRQPLGVSAGHDEDVCHFVLATSHIVSAGGDG

       310        320        330        340        350        360
KIGLGKIHSTFAAKYWAHEQEVNCVDCKGGIISFGSRDRTAKVWPLASGQLGQCLYTIQT

       370        380        390        400        410        420
EDQIWSVAIRPLLSSFVTGTACCGHFSPLKIWDLNSGQLMTHLDRDFPPRAGVLDVIYES

       430        440        450        460        470        480
PFALLSCGYDTYVRYWDCRTSVRKCVMEWEEPHNSTLYCLQTDGNHLLATGSSFYSVVRL

       490        500        510        520        530
WDRHQRACPHTFPLTSTRLGSPVYCLHLTTKHLYAALSYNLHVLDIQNP*
```

FIG.20A

```
        10         20         30         40         50         60         70         80         90
CGAGGGGGAAGCGAAGGAAGGGGAAGAGGAAGGGAAAAGCGAGCGAGAGGGGCAAGGCGGAAGAGGAAGCAGGGCGGAAGGGAAGCCCGGGCCG

    100        110        120        130        140        150        160        170        180
CAGACGGCGAAGGAGGCAGCGGGCCGGGGGCTGAGGCGGGAGCGAGGACACGCCCAAGAGAGGAAGCAGAGGGAGGCGGAAGCGTGGAGGAAGG

190        200        210        220        230        240        250        260        270        280
GGCGAGAGGCATCATCAAAGGAGATGAGGGGAGCGTAGGGGCCGGGAAAGAGGCACAAGGAAGAAAGTATGGGAAGGAGGAATGGAGGGTCAGG

      290        300        310        320        330        340        350        360        370
GCTAGGCGGCGGGAGGGCGCCAGGCCGGGAAGAGTACAAGGACAAGGAGGTCAGGTTTGGGCCTACATCCCGGGGACAGGGGCGGCCATGGCGG

 380        390        400        410        420        430        440        450        460        470
CGGCAGCCAGGGAGGAGGAGGAGGAGGCGGCTCGGGAGTCAGCCGCCTGCCCGGCTGCGGGGCCAGCGCTCTGGCGCCTGCCGGAAGTGCTGCT

        480        490        500        510        520        530        540        550        560
GCTGCACATGTGCTCCTACCTCGACATGCGGGCCCTCGGCCGCCTGGCCCAGGTGTACCGCTGGCTGTGGCACTTCACCAACTGCGACCTGCTC

    570        580        590        600        610        620        630        640        650
CGGCGCCAGATAGCCTGGGCCTCGCTCAACTCCGGCTTCACGCGGCTCGGCACCAACCTGATGACCAGTGTCCCAGTGAAGGTGTCTCAGAACT

660        670        680        690        700        710        720        730        740        750
GGATAGTGGGGTGCTGCCGAGAGGGGATTCTGCTGAAGTGGAGATGCAGTCAGATGCCCTGGATGCAGCTAGAGGATGATGCTTTGTACATATC

      760        770        780        790        800        810        820        830        840
CCAGGCTAATTTCATCCTGGCCTACCAGTTCCGTCCAGATGGTGCCAGCTTGAACCGTCAGCCTCTGGGAGTCTCTGCTGGGCATGATGAGGAC

 850        860        870        880        890        900        910        920        930        940
GTTTGCCACTTTGTGCTGGCCACCTCGCATATTGTCAGTGCAGGAGGAGATGGGAAGATTGGCCTTGGTAAGATTCACAGCACCTTCGCTGCCA
```

FIG.20B

```
        950         960         970         980         990        1000        1010        1020        1030
AGTACTGGGCTCATGAACAGGAGGTGAACTGTGTGGATTGCAAAGGGGGCATCATATCATTTGGCTCCAGGGACAGGACGGCCAAGGTGTGGCC

   1040        1050        1060        1070        1080        1090        1100        1110        1120
TTTGGCCTCAGGCCAGCTGGGGCAGTGTTTATACACCATCCAGACTGAAGACCAAATCTGGTCTGTTGCTATCAGGCCATTACTCAGCTCTTTT

1130        1140        1150        1160        1170        1180        1190        1200        1210        1220
GTGACAGGGACGGCTTGTTGTGGGCACTTCTCACCCCTGAAAATCTGGGACCTCAACAGTGGGCAGCTGATGACACACTTGGACAGAGACTTTC

     1230        1240        1250        1260        1270        1280        1290        1300        1310
CCCCAAGGGCTGGGGTGCTGGATGTCATATATGAGTCCCCTTTCGCACTGCTCTCCTGTGGCTATGACACCTATGTTCGCTACTGGGACTGCCG

 1320        1330        1340        1350        1360        1370        1380        1390        1400        1410
CACCAGTGTCCGGAAATGTGTCATGGAGTGGGAGGAGCCCCACAACAGCACCCTGTACTGCCTGCAGACAGATGGCAACCACTTGCTTGCCACA

      1420        1430        1440        1450        1460        1470        1480        1490        1500
GGTTCCTCCTTCTATAGCGTTGTACGGCTGTGGGACCGGCACCAAAGGGCCTGCCCGCACACCTTCCCGCTGACGTCGACCCGCCTCGGCAGCC

   1510        1520        1530        1540        1550        1560        1570        1580        1590
CTGTGTACTGCCTGCATCTCACCACCAAGCATCTCTATGCTGCGCTGTCTTACAACCTCCACGTCCTGGATATTCAAAACCCGTGA
```

FIG.20C

```
        10         20         30         40         50         60
LILTSVLLFQRHGYCTLGEAFNRLDFSSAIQDIRTFNYVVKLLQLIAKSQLTSLSGVAQK

        70         80         90        100        110        120
NYFNILDKIVQKVLDDHHNPRLIKDLLQDLSSTLCILIRGVGKSVLVGNININWICRLETI

       130        140        150        160        170        180
LAWQQQLQDLQMTKQVNNGLTLSDLPLHMLNNILYRFSDGWDIITLGQVTPTLYMLSEDR

       190        200        210        220        230        240
QLWKKLCQYHFAEKQFCRHLILSEKGHIEWKLMYFALQKHYPAKEQYGDTLHFCRHCSIL

       250        260        270
FWKDSGHPCTAADPDSCFTPVSPQHFIDLFKF
```

FIG.21A

```
          10         20         30         40         50         60
GCATTGCTATAATTTTACTATACTCTCATCTAAATCTAAAATCAGTCTTCAAAATAAAAACAAATTGTC

70         80         90        100        110        120        130
CTTTGCCAAAAATTTTTTTAATCGCACAATTAATTGACATTAACTGCCAATTCTTTTTGGCTAATTGAC

140        150        160        170        180        190        200
TAATTTTAACTTCTGTGTTGCTTTTCCAGAGGCATGGCTATTGCACCTTGGGAGAAGCCTTTAATCGGT

210        220        230        240        250        260        270
TAGACTTCTCAAGTGCAATTCAAGATATCCGAACGTTCAATTATGTGGTCAAACTGTTGCAGCTAATTG

 280        290        300        310        320        330        340
CAAAATCCCAGTTAACTTCATTGAGTGGCGTGGCACAGAAGAATTACTTCAACATTTTGGATAAAATCG

 350        360        370        380        390        400        410
TTCAAAAGGTTCTTGATGACCACCACAATCCTCGCTTAATCAAAGATCTTCTGCAAGACCTAAGCTCTA

 420        430        440        450        460        470        480
CCCTCTGCATTCTTATTAGAGGAGTAGGGAAGTCTGTATTAGTGGGAAACATCAATATTTGGATTTGCC

 490        500        510        520        530        540        550
GATTAGAAACTATTCTCGCCTGGCAACAACAGCTACAGGATCTTCAGATGACTAAGCAAGTGAACAATG

 560        570        580        590        600        610        620
GCCTCACCCTCAGTGACCTTCCTCTGCACATGCTGAACAACATCCTATACCGGTTCTCAGACGGATGGG

 630        640        650        660        670        680        690
ACATCATCACCTTAGGCCAGGTGACCCCCACGTTGTATATGCTTAGTGAAGACAGACAGCTGTGGAAGA

 700        710        720        730        740        750
AGCTTTGTCAGTACCATTTTGCTGAAAAGCAGTTTTGTAGACATTTGATCCTTTCAGAAAAAGGTCATA

760        770        780        790        800        810        820
TTGAATGGAAGTTGATGTACTTTGCACTTCAGAAACATTACCCAGCGAAGGAGCAGTACGGAGACACAC

830        840        850        860        870        880        890
TGCATTTCTGTCGGCACTGCAGCATTCTCTTTTGGAAGGACTCAGGACACCCCTGCACGGCGGCCGACC

900        910        920        930        940        950        960
CTGACAGCTGCTTCACGCCTGTGTCTCCGCAGCACTTCATCGACCTCTTCAAGTTTTAAGGGCTGCCCC
```

FIG.21B

970 980 990 1000 1010 1020 1030
TGCCATCCCTATTGGAGATTGTGAATCCTGCTGTCTGTGCAGGGCTCATAGTGAGTGTTCTGTGAGGTG

1040 1050 1060 1070 1080 1090 1100
GGTGGAGACTCCTCGGAAGCCCCTGCTTCCAGAAAGCCTGGGAAGAACTGCCCTTCTGCAAAGGGGGGA

1110 1120 1130 1140 1150 1160 1170
CTGCATGGTTGCATTTTCATCACTGAAAGTCAGAGGCCAAGGAAATCATTTCTACTTCTTTAAAAACTC

1180 1190 1200 1210
CTTCTAAGCATATTAAAATGTGAAATTTTGCGTACTCTCTC

FIG.21C

```
        10         20         30         40         50         60
YGSEGKGSSSISSDVSSSTDHTPTKAQKNVATSEDSDLSMRTLSTPSPALICPPNLPGFQ

        70         80         90        100        110        120
NGRGSSTSSSSITGETVAMVHSPPPTRLTHPLIRLASRPQKEQASIDRLPDHSMVQIFSF

       130        140        150        160        170        180
LPTNQLCRCARVCRRWYNLAWDPRLWRTIRLTGETINVDRALKVLTRRLCQDTPNVCLML

       190        200        210        220        230        240
ETVTVSGCRRLTDRGLYTIAQCCPELRRLEVSGCYNISNEAVFDVVSLCPNLEHLDVSGC

       250        260        270        280        290        300
SKVTCISLTREASIKLSPLHGKQISIRYLDMTDCFVLEDEGLHTIAAHCTQLTHLYLRRC

       310        320        330        340        350        360
VRLTDEGLRYLVIYCASIKELSVSDCRFVSDFGLREIAKLESRLRYLSIAHCGRVTDVGI

       370        380        390        400        410        420
RYVAKYCSKLRYLNARGCEGITDHGVEYLAKNCTKLKSLDIGKCPLVSDTGLECLALNCF

       430        440        450        460        470        480
NLKRLSLKSCESITGQGLQIVAANCFDLQTLNVQDCEVSVEALRFVKRHCKRCVIEHTNP

AFF
```

FIG.22A

```
        10        20        30        40        50        60        70        80        90       100       110       120       130
AGTACGGCAGTGAGGGCAAAGGCAGCTCGAGCATCTCATCTGACGTGAGTTCAAGTACAGATCACACGCCCACTAAAGCCCAGAAGAATGTGGCTACCAGCGAAGACTCCGACCTGAGCATGCGCACACTGAGCACGCC

  140       150       160       170       180       190       200       210       220       230       240       250       260       270
CAGCCCAGCCCTGATATGTCCACCGAATCTCCCAGGATTTCAGAATGGAAGGGGCTCGTCCACCTCCTCGTCCTCCATCACCGGGGAGACGGTGGCCATGGTGCACTCCCCGCCCCCGACCCGCCTCACACACCCGCTC

  280       290       300       310       320       330       340       350       360       370       380       390       400       410
ATCCGGCTCGCCTCCAGACCCCAGAAGGAGCAGGCCAGCATAGACCGGCTCCCGGACCACTCCATGGTGCAGATCTTCTCCTTCCTGCCCACCAACCAGCTGTGCCGCTGCGCGCGAGTGTGCCGCCGCTGGTACAACC

  420       430       440       450       460       470       480       490       500       510       520       530       540       550
TGGCCTGGGACCCGCGGCTCTGGAGGACTATCCGCCTGACGGGCGAGACCATCAACGTGGACCGCGCCCTCAAGGTGCTGACCCGCAGACTCTGCCAGGACACCCCCAACGTGTGTCTCATGCTGGAAACCGTAACTGT

  560       570       580       590       600       610       620       630       640       650       660       670       680       690
CAGTGGCTGCAGGCGGCTCACAGACCGAGGGCTGTACACCATCGCCCAGTGCTGCCCCGAACTGAGGCGACTGGAAGTCTCAGGCTGTTACAATATCTCCAACGAGGCCGTCTTTGATGTGGTGTCCCTCTGCCCTAAT

  700       710       720       730       740       750       760       770       780       790       800       810       820       830
CTGGAGCACCTGGATGTGTCAGGATGCTCCAAAGTGACCTGCATCAGCTTGACCCGGGAGGCCTCCATTAAACTGTCACCCTTGCATGGCAAACAGATTTCCATCCGCTACCTGGACATGACGGACTGCTTCGTGCTGG

  840       850       860       870       880       890       900       910       920       930       940       950       960       970
AGGACGAAGGCCTGCACACCATCGCGGCGCACTGCACGCAGCTCACCCACCTCTACCTGCGCCGCTGCGTCCGCCTGACCGACGAAGGCCTGCGCTACCTGGTGATCTACTGCGCCTCCATCAAGGAGCTGAGCGTCAG

  980       990      1000      1010      1020      1030      1040      1050      1060      1070      1080      1090      1100      1110
CGACTGCCGCTTCGTCAGCGACTTCGGCCTGCGGGAGATCGCCAAGCTGGAGTCCCGCCTGCGGTACCTGAGCATCGCGCACTGCGGCCGGGTCACCGACGTGGGCATCCGCTACGTGGCCAAGTACTGCAGCAAGCTG

 1120      1130      1140      1150      1160      1170      1180      1190      1200      1210      1220      1230      1240      1250
CGCTACCTCAACGCGAGGGGCTGCGAGGGCATCACGGACCACGGTGTGGAGTACCTCGCCAAGAACTGCACCAAACTCAAATCCCTGGATATCGGCAAATGCCCTTTGGTATCCGACACGGGCCTGGAGTGCCTGGCCC

 1260      1270      1280      1290      1300      1310      1320      1330      1340      1350      1360      1370      1380      1390
TGAACTGCTTCAACCTCAAGCGGCTCAGCCTCAAGTCCTGCGAGAGCATCACCGGCCAGGGCTTGCAGATCGTGGCCGCCAACTGCTTTGACCTCCAGACGCTGAATGTCCAGGACTGCGAGGTCTCCGTGGAGGCCCT
```

FIG.22B

1400 1410 1420 1430 1440 1450 1460 1470 1480 1490 1500 1510 1520
GCGCTTTGTCAAACGCCACTGCAAGCGCTGCGTCATCGAGCACACCAACCCGGCTTTCTTCTGAAGGGACAGAGTTCATCCGGCGTTGTATTCACACAAACCTGAACAAAGCAAATTTTTTTAAAAGCAGCGTATGTAA

1530 1540 1550 1560 1570 1580 1590 1600 1610 1620 1630 1640 1650 1660
GCACCGACACCCACTCAAAACAGCTCTTTCTTCCGGGAAGGTTATTAGGAATCTGGCCTTTATTTTTCCTCATTTCTCATGGGCAACAGAGGCCAAAGAAACGAAGCAAGACAAACAGCAAACAGGCATTTTGGTCAGG

1670 1680 1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
TCATTTGTAGGCAGTTTCTCTTCTCACAAAAGATGTACTTAAGCAGGCTGATCGCTGTTCCTTGAGCAAGGCGCTTACTCTCCTCCGCTCAGGCCCCCAAGGCCGCCCTTTCCCTCGCACACAGGCCCCACCCCCACAG

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920 1930 1940
TTCCACGCCCCCCCCCCAAGGCCACACCCTCCCTCCCTAGAGCAGCAGCGAGGATCCATCATCAGAATCACAGTGCTCTCCAGACCTCCTCTCTAAACTGCTTCATTGACCTAAGTCACTCTCTTCAATCCCACACCCA

1950 1960 1970 1980 1990 2000 2010 2020 2030 2040 2050 2060 2070 2080
TGGACATTCTTGTCAACTCAATACCATAGCACTTTGCATAGGCAAAATACTTTTCAGGCCTTTTTAAAAAATTCATTACAGCAAACAGCTGGGGAAGGACATGCAGTCCTCCCCCAGCTCTGTCAATGACTATGACCTT

2090 2100 2110 2120 2130 2140 2150 2160 2170 2180 2190 2200 2210 2220
GGCCAAAGCACTTCACTGCTCTGGGCTGCAGCTTCCAGCACTGAATCAGAGGCCACACAGCCCAAAGATTAGCTTCATGTCCATTATAGCATTGAGGGAGCAGAGATACCCATACACAGAAGCACCTTGGCATAGAGCA

2230 2240 2250 2260 2270 2280 2290 2300 2310 2320 2330 2340 2350 2360
CCCAGGCATCGACCTCTTCCAGGAGAACTGATTCTGTGGATGGATGTGATTTCAGGAGATTGTGCAGTGCCAGCATCAGTOCATAAAGGGTCCTGTATGTCCTTTGGCTGCAAATCACCCACTTCCCTGTGTTTCAGTG

2370 2380 2390 2400 2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
GGAGAATTTCCTCTCCCACCTCCTCACATCCTCTTTTGCCAGGCTGGATGCTGTCGTCTCTGTACACAAATACTTTCTGCATTCCCCCCTCCACACCATCCTAGCGAGGCACCAGCACACCTAATCACAGCAAAGCCCA

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600 2610 2620 2630 2640
GATCCCCCCATCAGTTGCTTTTACTCAGTGTTTTCAAATAGGAGTAAAGGCCCTTGCAATTTTTAATTAACAAGCAAGGCCCAAGGGAACACATGTCCTCAAAAGTTTTTCTGATCCCTCGCCTTGCACACCTGGCATG

2650 2660 2670 2680 2690 2700 2710 2720 2730 2740 2750 2760 2770 2780
CATCAGGCACATCTGTCCTACAGCTGGCAGAGACAGATGCCTCGGTTCTTTGTCATTCAGATTGCATTTGACCTCTTCTCATCTATTTATTTCTTTATACATCCAGACTTCATCACATGAAGCCTATTGGGGTTAAGTT

FIG.22C

2790 2800 2810 2820 2830 2840 2850 2860 2870 2880 2890 2900 2910
TGTAAGTGTTTAATTGTGCAAATTGCCACCCTGTGTACCTCCTCCATGTCTGTCTGCGTGTTTTCCACCAAAGAATGCAAAGCAGACTTCCAGGTGTTTAAATTCTGTTCACTCAACAATGCCAGATGAATGGAAGAGG

2920 2930 2940 2950 2960 2970 2980 2990 3000 3010 3020 3030 3040 3050
GAACACACTGAGATGACTTAGACTCTGGTCCACCAACCAGACCCTTGGAAAGGAATACTAAAATCATTACAAGGTATGGATTTTAAATGGATGAAACTTCAAATTATCTTATTTGGATAGAAGTCTATATTCTAGCCTC

3060 3070 3080 3090 3100 3110 3120 3130 3140 3150 3160 3170 3180 3190
ATTTGCATGAAGTCAGATAGCCAGAAGAAATTCCATTGCTGGTTTTCACGAAATTCACTTGTCTTTTGCTAATAAACACATGGCCCTTTCCCAGATTATTCTCTAGCCAAGCCCCACCTTTGTTACGTTGAAATCCCTC

3200 3210 3220 3230 3240 3250 3260 3270 3280 3290 3300 3310 3320 3330
ATTTATTTTCTTCTCAAAATGCCCATTATCCAAATGCAGAACCTCTGCATCTCCAAGCCAGTTATGCTGAATTTGTCAAACTTAGACACCCTTGACAACTGCACTCCTACTGTAGGCTCCTGTGCATACTGTCGTCTTC

3340 3350 3360 3370 3380 3390 3400 3410 3420 3430 3440 3450 3460 3470
TGTGGGGGATGGAGAGGTTAGTGTGATGAGGTGGTGTCTGCCCAGGAGGTTTCTTTCAAACATCATGGCCTCCCATCCAATCAACATCATCAAATTACATGTGTAATCAAGGCTCTGTGCCATGGGGGAAATGAATCAT

3480 3490 3500 3510 3520 3530 3540 3550 3560 3570 3580 3590 3600 3610
TTAGCTAGGCCAGGATCTAGTGAAAGCCACAGAGTTTAAAACCATGAAAGAAGTTGAAGGCAGCATTCCTCAGCTCTGTGACTTGTGACCCTATTTGAAGTTTCAGGATTTGGGTGTCACAAAGGATTGTCCCTAATCC

3620 3630 3640 3650 3660 3670 3680 3690 3700 3710 3720 3730 3740 3750
TTGGCCCTGGGGTCTTCCGAGTGAGCTGGTTTAATACTCTGAGAATGAGCAGGGAGATCCAGAGAATGAATCCCTGACCGCATCACCTAAACTGTCTTCCAAACATGAGACAAAGCTGACTGTTCACACTGATTGCCCA

3760 3770 3780 3790 3800 3810 3820 3830 3840 3850 3860 3870 3880 3890
GCACATACCGTCTTGCCAGTTTCTTCTTTTCTCCCAGTCTCCTGTTCATCCATTCTGTTCTCCCTTGGGGTGGGAATCTATGATGGAGGTTACTGGGGAAACAGCTCAGCAGATTTTTGGAGACCAAACCAAAGGTCTC

3900 3910 3920 3930 3940 3950 3960 3970 3980 3990 4000 4010 4020 4030
ACTAGGAAATTTATCTGTTTTAAAACATTGCTTCCTTCCTGGCTCTGCTAAATTGAATGCTCATTGTTTGTTGTTGTTTTTTAATTCTAATGTTCAAATCACTGCGTGCTGTATGAATCTAGAAAGCCTTAATTTA

4040 4050
CTACCAAGAAATAAAGCAATATGTTCGT

FIG.22D

```
        10         20         30         40         50         60
AAAPAPAPAPTPTPEEGPDAGWGDRIPLEILVQIFGLLVAADGPMPFLGRAARVCRRWQE

        70         80         90        100        110        120
AASQPALWHTVTLSSPLVGRPAKGGVKAEKKLLASLEWLMPNRFSQLQRLTLIHWKSQVH

       130        140        150        160        170        180
PVLKLVGECCPRLTFLKLSGCHGVTADALVMLAKACCQLHSLDLQHSMVESTAVVSFLEE

       190        200        210        220        230        240
AGSRMRKLWLTYSSQTTAILGALLGSCCPQLQVLEVSTGINRNSIPLQLPVEALQKGCPQ

       250        260        270        280
LQVLRLLNLMWLPKPPGRGVAPGPGFPSLEELCLASSTCNFVS
```

FIG.23A

```
          10         20         30         40         50         60
TGCGGCCGCGCCCGCACCCGCACCGGCACCCACGCCCACGCCCGAGGAAGGGCCCGACGCGGGCTGGGG

70         80         90        100        110        120        130
AGACCGCATTCCCTTGGAAATCCTGGTGCAGATTTTCGGGTTGTTGGTGGCGGCGGACGGCCCCATGCC

140        150        160        170        180        190        200
CTTCCTGGGCAGGGCTGCGCGCGTGTGCCGCCGCTGGCAGGAGGCCGCTTCCCAACCCGCGCTCTGGCA

210        220        230        240        250        260        270
CACCGTGACCCTGTCGTCCCCGCTGGTCGGCCGGCCTGCCAAGGGCGGGGTCAAGGCGGAGAAGAAGCT

 280        290        300        310        320        330        340
CCTTGCTTCCCTGGAGTGGCTTATGCCCAATCGGTTTTCACAGCTCCAGAGGCTGACCCTCATCCACTG

 350        360        370        380        390        400        410
GAAGTCTCAGGTACACCCCGTGTTGAAGCTGGTAGGTGAGTGCTGTCCTCGGCTCACTTTCCTCAAGCT

 420        430        440        450        460        470        480
CTCCGGCTGCCACGGTGTGACTGCTGACGCTCTGGTCATGCTAGCCAAAGCCTGCTGCCAGCTCCATAG

 490        500        510        520        530        540        550
CCTGGACCTACAGCACTCCATGGTGGAGTCCACAGCTGTGGTGAGCTTCTTGGAGGAGGCAGGGTCCCG

 560        570        580        590        600        610        620
AATGCGCAAGTTGTGGCTGACCTACAGCTCCCAGACGACAGCCATCCTGGGCGCATTGCTGGGCAGCTG

 630        640        650        660        670        680        690
CTGCCCCCAGCTCCAGGTCCTGGAGGTGAGCACCGGCATCAACCGTAATAGCATTCCCCTTCAGCTGCC

 700        710        720        730        740        750
TGTCGAGGCTCTGCAGAAAGGCTGCCCTCAGCTCCAGGTGCTGCGGCTGTTGAACCTGATGTGGCTGCC

760        770        780        790        800        810        820
CAAGCCTCCGGGACGAGGGGTGGCTCCCGGACCAGGCTTCCCTAGCCTAGAGGAGCTCTGCCTGGCGAG

830        840        850
CTCAACCTGCAACTTTGTGAGC
```

FIG.23B

```
        10         20         30         40         50         60
QHCSQKDTAELLRGLSLWNHAEERQKFFKYSVDEKSDKEAEVSEHSTGITHLPPEVMLSI

        70         80         90        100        110        120
FSYLNPQELCRCSQVSMKWSQLTKTGSLWKHLYPVHWARGDWYSGPATELDTEPDDEWVK

       130        140        150        160        170        180
NRKDESRAFHEWDEDADIDESEESAEESIAISIAQMEKRLLHGLIHNVLPYVGTSVKTLV

       190        200        210        220        230        240
LAYSSAVSSKMVRQILELCPNLEHLDLTQTDISDSAFDSWSWLGCCQSLRHLDLSGCEKI

       250        260        270        280        290        300
TDVALEKISRALGILTSHQSGFLKTSTSKITSTAWKNKDITMQSTKQYACLHDLTNKGIG

       310        320        330        340        350        360
EEIDNEHPWTKPVSSENFTSPYVWMLDAEDLADIEDTVEWRHRNVESLCVMETASNFSCS

       370        380        390        400        410        420
TSGCFSKDIVGLRTSVCWQQHCASPAFAYCGHSFCCTGTALRTMSSLPESSAMCRKAART

       430        440        450        460        470        480
RLPRGKDLIYFGSEKSDQETGRVLLFLSLSGCYQITDHGLRVLTLGGGLPYLEHLNLSGC

       490        500        510        520        530        540
LTITGAGLQDLVSACPSLNDEYFYYCDNINGPHADTASGCQNLQCGFRACCRSGE*PLTS

       550        560        570        580        590
DLCLLHLAEQAFFHALYS*HISCVNHPFLSVTCFGPIXYNFRNLNYQXIVML
```

FIG.24A

```
        10         20         30         40         50         60         70         80         90
ACAACACTGCTCTCAGAAGGATACTGCAGAACTCCTTAGAGGTCTTAGCCTATGGAATCATGCTGAAGAGCGACAGAARTTTTTTAAATATTCC

    100        110        120        130        140        150        170        180
GTGGATGAAAAGTCAGATAAAGAAGCAGAAGTGTCAGAACACTCCACAGGTATAACCCATCTTCCTCCTGAGGTAATGCTGTCAATTTTCAGCT

190        200        210        220        230        240        250        260        270        280
ATCTTAATCCTCAAGAGTTATGTCGATGCAGTCAAGTAAGCATGAAATGGTCTCAGCTGACAAAAACGGGATCGCTTTGGAAACATCTTTACCC

     290        300        310        320        330        340        350        360        370
TGTTCATTGGGCCAGAGGTGACTGGTATAGTGGTCCCGCAACTGAACTTGATACTGAACCTGATGATGAATGGGTGAAAAATAGGAAAGATGAA

 380        390        400        410        420        430        440        450        460        470
AGTCGTGCTTTTCATGAGTGGGATGAAGATGCTGACATTGATGAATCTGAAGAGTCTGCGGAGGAATCAATTGCTATCAGCATTGCACAAATGG

        480        490        500        510        520        530        540        550        560
AAAAACGTTTACTCCATGGCTTAATTCATAACGTTCTACCATATGTTGGTACTTCTGTAAAAACCTTAGTATTAGCATACAGCTCTGCAGTTTC

    570        580        590        600        610        620        630        640        650
CAGCAAAATGGTTAGGCAGATTTTAGAGCTTTGTCCTAACCTGGAGCATCTGGATCTTACCCAGACTGACATTTCAGATTCTGCATTTGACAGT

660        670        680        690        700        710        720        730        740        750
TGGTCTTGGCTTGGTTGCTGCCAGAGTCTTCGGCATCTTGATCTGTCTGGTTGTGAGAAAATCACAGATGTGGCCCTAGAGAAGATTTCCAGAG

     760        770        780        790        800        810        820        830        840
CTCTTGGAATTCTGACATCTCATCAAAGTGGCTTTTTGAAAACATCTACAAGCAAAATTACTTCAACTGCGTGGAAAAATAAAGACATTACCAT

 850        860        870        880        890        900        910        920        930        940
GCAGTCCACCAAGCAGTATGCCTGTTTGCACGATTTAACTAACAAGGGCATTGGAGAAGAAATAGATAATGAACACCCCTGGACTAAGCCTGTT
```

FIG.24B

```
        950        960        970        980        990       1000       1010       1020       1030
TCTTCTGAGAATTTCACTTCTCCTTATGTGTGGATGTTAGATGCTGAAGATTTGGCTGATATTGAAGATACTGTGGAATGGAGACATAGAAATG

   1040       1050       1060       1070       1080       1090       1100       1110       1120
TTGAAAGTCTTTGTGTAATGGAAACAGCATCCAACTTTAGTTGTTCCACCTCTGGTTGTTTTAGTAAGGACATTGTTGGACTAAGGACTAGTGT

1130       1140       1150       1160       1170       1180       1190       1200       1210       1220
CTGTTGGCAGCAGCATTGTGCTTCTCCAGCCTTTGCGTATTGTGGTCACTCATTTTGTTGTACAGGAACAGCTTTAAGAACTATGTCATCACTC

     1230       1240       1250       1260       1270       1280       1290       1300       1310
CCAGAATCTTCTGCAATGTGTAGAAAAGCAGCAAGGACTAGATTGCCTAGGGGAAAAGACTTAATTTACTTTGGGAGTGAAAAATCTGATCAAG

1320       1330       1340       1350       1360       1370       1380       1390       1400       1410
AGACTGGACGTGTACTTCTGTTTCTCAGTTTATCTGGATGTTATCAGATCACAGACCATGGTCTCAGGGTTTTGACTCTGGGAGGAGGGCTGCC

      1420       1430       1440       1450       1460       1470       1480       1490       1500
TTATTTGGAGCACCTTAATCTCTCTGGTTGTCTTACTATAACTGGTGCAGGCCTGCAGGATTTGGTTTCAGCATGTCCTTCTCTGAATGATGAA

  1510       1520       1530       1540       1550       1560       1570       1580       1590
TACTTTTACTACTGTGACAACATTAACGGTCCTCATGCTGATACCGCCAGTGGATGCCAGAATTTGCAGTGTGGTTTTCGAGCCTGCTGCCGCT

1600       1610       1620       1630       1640       1650       1660       1670       1680       1690
CTGGCGAATGACCCTTGACTTCTGATCTTTGTCTACTTCATTTAGCTGAGCAGGCTTTCTTTCATGCACTTTACTCATAGCACATTTCTTGTGT

     1700       1710       1720       1730       1740       1750       1760       1770
TAACCATCCCTTTTTGAGCGTGACTTGTTTTGGGCCCATTNYTTACAACTTCAGAAATCTTAATTACCAGTGRATTGTAATGTTG
```

FIG.24C

```
        10         20         30         40         50         60
RVTSGCGLARGSSAMVFSNNDEGLINKKLPKELLLRIFSFLDIVTLCRCAQISKAWNILA

        70         80         90        100        110        120
LDGSNWQRIDLFNFQIDVEGRVVENISKRCVGFLRKLSLRGCIGVGDSSLKTFAQNCRNI

       130        140        150        160        170        180
EHLNLNGCTKITDSTCYSLSRFCSKLKHLXLTSCVSITNSSLKGISEGCRNLEYLNLSWC

       190        200        210        220        230        240
DQITKDGIEALVRGCRGLKALLLRGCTQLEDEALKHIQNYCHELVSLNLQSCSRITDEGV

       250        260        270        280        290        300
VQICRGCHRLQALCLSGCSNLTDASLTALGLNCPRLQILEAARCSHLTDAGFTLLARNCH

       310        320        330        340        350        360
ELEKMDLEXCILITDSTLIQLSIHCPKLQALSLSHCELIXDDGILHLSNSTCGHERLRVL

       370        380        390        400        410        420
ELDNCLLITDVALXHLENCRGLERLELYDCQQVTRAGIKRMRAQLPHVKVHAYFAPVTPP

       430        440        450        460        470        480
TAVAGSGQRLCRCCVIL*QQLPGPKG**GILSSRRPESS*PTPPSPNLLILHWERHLQFP

       490        500        510        520        530        540
NRHLSRFKNGEDKKGFISNI*HHIVT*NMALT*LVLLLPSSLMSSLTSTHLLL*YL*RLI

       550
ILKTDQTGPASKYINCVQ*
```

FIG.25A

```
        10         20         30         40         50         60         70         80         90
TTTTACTGTACACAGTTGATGTATTTTGATGCTGGGCCTGTCTGGTCTGTCTTGAGGATTATTAACCTTTAGAGGTATCAGAGAAGCAAATGGG

   100        110        120        130        140        150        160        170        180
TACTGGTGAGGCTGCTCATTAGGGAAGAGGGCAAAAGGAGCACTAGCTAGGTCAGAGCCATGTTTCAGGTCACAATGTGATGTCAGATGTTGCT

190        200        210        220        230        240        250        260        270        280
TATAAATCCTTTCTTGTCTTCGCCATTCTTAAATCTTGATAGGTGCCTGTTGGGAAACTGTAAATGCCTTTCCCAATGGAGAATCAACAGATTG

     290        300        310        320        330        340        350        360        370
GGTGATGGTGGAGTCGGTCAGGAAGACTCAGGTCTTCTAGAGGAAAGGATGCCTCATCACCCCTTNGGCCCAGGCAGCTGCTGTCAGAGAATGA

 380        390        400        410        420        430        440        450        460        470
CACAGCACCTGCACAGTCGCTGTCCACTTCCTGCCACTGCTGTCGGTGGGGTGACGGGAGCAAAGTAGGCGTGGACTTTGACATGAGGGAGCTG

        480        490        500        510        520        530        540        550        560
AGCCCGCATCCGCTTGATGCCTGCACGGGTAACCTGCTGGCAGTCGTACAGCTCGAGGCGCTCCAGGCCTCGGCAGTTCTCTAGGTGTYCCAGG

   570        580        590        600        610        620        630        640        650
GCCACATCAGTGATGAGGAGGCAGTTGTCCAACTCCAGTACCCGCAGCCTCTCATGGCCACAGGTACTGTTGCTCAGGTGCAGGATCCCATCAT

660        670        680        690        700        710        720        730        740        750
CTGKGATGAGTTCACAGTGGGACAGGCTCAGGGCTTGCAGTTTAGGACAGTGAATGGAGAGCTGGATGAGTGTGCTGTCGGTTATCAGGATGCA

     760        770        780        790        800        810        820        830        840
WTCTTCAAGATCCATCTTCTCCAATTCGTGGCAATTCCGAGCTAAAAGTGTAAAACCTGCGTCAGTCAAATGGGAGCATCGGGCAGCCTCCAAA
```

FIG.25B

850 860 870 880 890 900 910 920 930 940
ATTTGCAGTCGCGGACAGTTCAAACCCAGGGCTGTAAGAGAGGCATCTGTGAGGTTGCTGCAACCCGAAAGGCAGAGAGCCTGTAGCCGGTGAC

950 960 970 980 990 1000 1010 1020 1030
AGCCCCTGCATATCTGCACCACACCTTCATCCGTGATACGTGAGCAGGACTGCAAGTTGAGGCTCACAAGCTCATGGCAGTAATTCTGAATGTG

1040 1050 1060 1070 1080 1090 1100 1110 1120
TTTCAGAGCTTCATCTTCTAACTGTGTGCAGCCCCTCAGGAGCAGGGCTTTCAGGCCTCGACAACCTCGCACCAGTGCCTCGATGCCATCCTTC

1130 1140 1150 1160 1170 1180 1190 1200 1210 1220
GTGATCTGATCACACCAAGAGAGGTTCAGGTACTCCAGGTTTCGGCAGCCCTCACTGATCCCCTTCAAGGAGCTGTTTGTAATAGACACACAGG

1230 1240 1250 1260 1270 1280 1290 1300 1310
AGGTCAGAWCCAGATGTTTCAGCTTGGAACAGAATCTGCTAAGGCTATAACACGTGCTGTCAGTGATTTTTGTGCATCCATTGAGGTTCAAATG

1320 1330 1340 1350 1360 1370 1380 1390 1400 1410
TTCAATGTTTCGGCAGTTCTGTGCAAAGGTCTTCAAGGAGGAATCCCCAACACCAATGCAGCCTCGCAAGCTGAGCTTCCTCAGGAATCCAACG

1420 1430 1440 1450 1460 1470 1480 1490 1500
CATCGCTTCGAGATATTTTCCACCACTCGACCCTCTACATCTATTTGAAAGTTAAAAAGATCTATTCTTTGCCAGTTGCTTCCATCCAGGGCTA

1510 1520 1530 1540 1550 1560 1570 1580 1590
AGATGTTCCAAGCCTTGGAAATCTGTGCACATCGGCACAAAGTTACTATATCCAAGAAGGAAAATATTCTTAACAGAAGTTCTTTGGGTAACTT

1600 1610 1620 1630 1640 1650 1660 1670 1680
TTTGTTAATAAGGCCTTCATCATTGTTTGAGAAAACCATGGCCGAAGAGCCGCGAGCGAGCCCACAGCCCGAAGTCACACGGC

FIG.25C

```
        10         20         30         40         50         60
MSPVFPMLTVLTMFYYICLRRRARTATRGEMMNTHRAIESNSQTSPLNAEVVQYAKEVVD

        70         80         90        100        110        120

FSSHYGSENSMSYTMWNLAGVPNVFPSSGDFTQTAVFRTYGTWWDQCPSASLPFKRTPPN

       130        140        150        160        170        180
FQSQDYVELTFEQQVYPTAVHVLETYHPGAVIRILACSANPYSPNPPAEVRWEILWSERP

       190        200        210        220        230        240
TKVNASQARQFKPCIKQINFPTNLIRLEVNSSLLEYYTELDAVVLHGVKDKPVLSLKTSL

       250        260        270        280        290        300
IDMNDIEDDAYAEKDGCGMDSLNKKFSSAVLGEGPNNGYFDKLPYELIQLILNHLTLPDL

       310        320        330        340        350        360
CRLAQTCKLLSQHCCDPLQYIHLNLQPYWAKLDDTSLEFLQSRCTLVQWLNLSWTGNRGF

       370        380        390        400        410        420
ISVAGFSRFLKVCGSELVRLELSCSHFLNETCLEVISEMCPNLQALNLSSCDKLPPQAFN

       430        440        450        460        470        480
HIAKLCSLKRLVLYRTKVEQTALLSILNFCSELQHLSLGSCVMIEDYDVIASMIGAKCKK

       490        500        510        520        530        540
LRTLDLWRCKNITENGIAELASGCPLLEELDLGWCPTLQSSTGCFTRLAHQLPNLQKLFL

       550        560        570        580        590        600
TANRSVCDTDIDELACNCTRLQQLDILGTRMVSPASLRKLLESCKDLSLLDVSFCSQIDN

       610        620
RAVLELNASFPKVFIKKSFTQ
```

FIG.26A

```
        10         20         30         40         50         60         70         80         90
ATGTCACCGGTCTTTCCCATGTTAACAGTTCTGACCATGTTTTATTATATATGCCTTCGGCGCCGAGCCAGGACAGCTACAAGAGGAGAAATGA

    100        110        120        130        140        150        160        170        180
TGAACACCCATAGAGCTATAGAATCAAACAGCCAGACTTCCCCTCTCAATGCAGAGGTAGTCCAGTATGCCAAAGAAGTAGTGGATTTCAGTTC

190        200        210        220        230        240        250        260        270        280
CCATTATGGAAGTGAGAATAGTATGTCCTATACTATGTGGAATTTGGCTGGTGTACCAAATGTATTCCCAAGTTCTGGTGACTTTACTCAGACA

      290        300        310        320        330        340        350        360        370
GCTGTGTTTCGAACTTATGGGACATGGTGGGATCAGTGTCCTAGTGCTTCCTTGCCATTCAAGAGGACGCCACCTAATTTTCAGAGCCAGCACT

 380        390        400        410        420        430        440        450        460        470
ATGTGGAACTTACTTTTGAACAACAGGTGTATCCTACAGCTGTACATGTTCTAGAAACCTATCATCCCGGAGCAGTCATTAGAATTCTCGCTTG

        480        490        500        510        520        530        540        550        560
TTCTGCAAATCCTTATTCCCCAAATCCACCAGCTGAAGTAAGATGGGAGATTCTTTGGTCAGAGAGACCTACGAAGGTGAATGCTTCCCAAGCT

    570        580        590        600        610        620        630        640        650
CGCCAGTTTAAACCTTGTATTAAGCAGATAAATTTCCCCACAAATCTTATACGACTGGAAGTAAATAGTTCTCTTCTGGAATATTACACTGAAT

660        670        680        690        700        710        720        730        740        750
TAGATGCAGTTGTGCTACATGGTGTGAAGGACAAGCCAGTGCTTTCTCTCAAGACTTCACTTATTGACATGAATGATATAGAAGATGATGCCTA

      760        770        780        790        800        810        820        830        840
TGCAGAAAAGGATGGTTGTGGAATGGACAGTCTTAACAAAAAGTTTAGCAGTGCTGTCCTCGGGGAAGGGCCAAATAATGGGTATTTTGATAAA

 850        860        870        880        890        900        910        920        930        940
CTACCTTATGAGCTTATTCAGCTGATTCTGAATCATCTTACACTACCAGACCTGTGTAGATTAGCACAGACTTGCAAACTACTGAGCCAGCATT
```

FIG.26B

```
       950        960        970        980        990       1000       1010       1020       1030
GCTGTGATCCTCTGCAATACATCCACCTCAATCTGCAACCATACTGGGCAAAACTAGATGACACTTCTCTGGAATTTCTACAGTCTCGCTGCAC

  1040       1050       1060       1070       1080       1090       1100       1110       1120
TCTTGTCCAGTGGCTTAATTTATCTTGGACTGGCAATAGAGGCTTCATCTCTGTTGCAGGATTTAGCAGGTTTCTGAAGGTTTGTGGATCCGAA

1130       1140       1150       1160       1170       1180       1190       1200       1210       1220
TTAGTACGCCTTGAATTGTCTTGCAGCCACTTTCTTAATGAAACTTGCTTAGAAGTTATTTCTGAGATGTGTCCAAATCTACAGGCCTTAAATC

    1230       1240       1250       1260       1270       1280       1290       1300       1310
TCTCCTCCTGTGATAAGCTACCACCTCAAGCTTTCAACCACATTGCCAAGTTATGCAGCCTTAAACGACTTGTTCTCTATCGAACAAAAGTAGA

1320       1330       1340       1350       1360       1370       1380       1390       1400       1410
GCAAACAGCACTGCTCAGCATTTTGAACTTCTGTTCAGAGCTTCAGCACCTCAGTTTAGGCAGTTGTGTCATGATTGAAGACTATGATGTGATA

      1420       1430       1440       1450       1460       1470       1480       1490       1500
GCTAGCATGATAGGAGCCAAGTGTAAAAAACTCCGGACCCTGGATCTGTGGAGATGTAAGAATATTACTGAGAATGGAATAGCAGAACTGGCTT

  1510       1520       1530       1540       1550       1560       1570       1580       1590
CTGGGTGTCCACTACTGGAGGAGCTTGACCTTGGCTGGTGCCCAACTCTGCAGAGCAGCACCGGGTGCTTCACCAGACTGGCACACCAGCTCCC

1600       1610       1620       1630       1640       1650       1660       1670       1680       1690
AAACTTGCAAAAACTCTTTCTTACAGCTAATAGATCTGTGTGTGACACAGACATTGATGAATTGGCATGTAATTGTACCAGGTTACAGCAGCTG

    1700       1710       1720       1730       1740       1750       1760       1770       1780
GACATATTAGGAACAAGAATGGTAAGTCCGGCATCCTTAAGAAAACTCCTGGAATCTTGTAAAGATCTTTCTTTACTTGATGTGTCCTTCTGTT

1790       1800       1810       1820       1830       1840       1850       1860
CGCAGATTGATAACAGAGCTGTGCTAGAACTGAATGCAAGCTTTCCAAAAGTGTTCATAAAAAAGAGCTTTACTCAGTGA
```

FIG.26C

```
        10         20         30         40         50         60
MQLVPDIEFKITYTRSPDGDGVGNSYIEDNDDDSKMADLLSYFQQQLTFQESVLKLCQPE

        70         80         90        100        110        120
LESSQIHISVLPMEVLMYIFRWVVSSDLDLRSLEQLSLVCRGFYICARDPEIWRLACLKV

       130        140        150        160        170        180
WGRSCIKLVPYTSWREMFLERPRVRFDGVYISKTTYIRQGEQSLDGFYRAWHQVEYYRYI

       190        200        210        220        230        240
RFFPDGHVMMLTTPEEPQSIVPRLRTRNTRTDAILLGHYRLSQDTDNQTKVFAVITKKKE

       250        260        270        280        290        300
EKPLDYKYRYFRRVPVQEADQSFHVGLQLCSSGHQRFNKLIWIHHSCHITYKSTGETAVS

       310        320
AFEIDKMYTPLFFARVRSYTAFSERPL
```

FIG.27A

```
          10         20         30         40         50         60
ATGCAACTTGTACCTGATATAGAGTTCAAGATTACTTATACCCGGTCTCCAGATGGTGATGGCGTTGGA

70         80         90        100        110        120        130
AACAGCTACATTGAAGATAATGATGATGACAGCAAAATGGCAGATCTCTTGTCCTACTTCCAGCAGCAA

140        150        160        170        180        190        200
CTCACATTTCAGGAGTCTGTGCTTAAACTGTGTCAGCCTGAGCTTGAGAGCAGTCAGATTCACATATCA

210        220        230        240        250        260        270
GTGCTGCCAATGGAGGTCCTGATGTACATCTTCCGATGGGTGGTGTCTAGTGACTTGGACCTCAGATCA

280        290        300        310        320        330        340
TTGGAGCAGTTGTCGCTGGTGTGCAGAGGATTCTACATCTGTGCCAGAGACCCTGAAATATGGCGTCTG

350        360        370        380        390        400        410
GCCTGCTTGAAAGTTTGGGGCAGAAGCTGTATTAAACTTGTTCCGTACACGTCCTGGAGAGAGATGTTT

420        430        440        450        460        470        480
TTAGAACGGCCTCGTGTTCGGTTTGATGGCGTGTATATCAGTAAAACCACATATATTCGTCAAGGGGAA

490        500        510        520        530        540        550
CAGTCTCTTGATGGTTTCTATAGAGCCTGGCACCAAGTGGAATATTACAGGTACATAAGATTCTTTCCT

560        570        580        590        600        610        620
GATGGCCATGTGATGATGTTGACAACCCCTGAAGAGCCTCAGTCCATTGTTCCACGTTTAAGAACTAGG

630        640        650        660        670        680        690
AATACCAGGACTGATGCAATTCTACTGGGTCACTATCGCTTGTCACAAGACACAGACAATCAGACCAAA

700        710        720        730        740        750
GTATTTGCTGTAATAACTAAGAAAAAAGAAGAAAAACCACTTGACTATAAATACAGATATTTTCGTCGT

760        770        780        790        800        810        820
GTCCCTGTACAAGAAGCAGATCAGAGTTTTCATGTGGGGCTACAGCTATGTTCCAGTGGTCACCAGAGG

830        840        850        860        870        880        890
TTCAACAAACTCATCTGGATACATCATTCTTGTCACATTACTTACAAATCAACTGGTGAGACTGCAGTC

900        910        920        930        940        950        960
AGTGCTTTTGAGATTGACAAGATGTACACCCCCTTGTTCTTCGCCAGAGTAAGGAGCTACACAGCTTTC

970        980
TCAGAAAGGCCTCTGTAG
```

FIG.27B

```
        10         20         30         40         50         60
AALDPDLENDDFFVRKTGAFHANPYVLRAFEDFRKFSEQDDSVERDIILQCREGELVLPD

        70         80         90        100        110        120
LEKDDMIVRRIPAQKKEVPLSGAPDRYHPVPFPEPWTLPPEIQAKFLCVLERTCPSKEKS

       130        140        150        160        170        180
NSCRILVPSYRQKKDDMLTRKIQSWKLGTTVPPISFTPGPCSEADLKRWEAIREASRLRH

       190        200        210        220        230        240
KKRLMVERLFQKIYGENGSKSMSDVSAEDVQNLRQLRYEEMQKIKSQLKEQDQKWQDDLA

       250
KWKDRRKSYTSDLQK
```

FIG.28A

```
          10         20         30         40         50         60
GCAGCCCTGGATCCTGACTTAGAGAATGATGATTTCTTTGTCAGAAAGACTGGGGCTTTCCATGCAAAT

70         80         90        100        110        120        130
CCATATGTTCTCCGAGCTTTTGAAGACTTTAGAAAGTTCTCTGAGCAAGATGATTCTGTAGAGCGAGAT

140        150        160        170        180        190        200
ATAATTTTACAGTGTAGAGAAGGTGAACTTGTACTTCCGGATTTGGAAAAAGATGATATGATTGTTCGC

210        220        230        240        250        260        270
CGAATCCCAGCACAGAAGAAAGAAGTGCCGCTGTCTGGGGCCCCAGATAGATACCACCCAGTCCCTTTT

 280        290        300        310        320        330        340
CCCGAACCCTGGACTCTTCCTCCAGAAATTCAAGCAAAATTTCTCTGTGTACTTGAAAGGACATGCCCA

  350        360        370        380        390        400        410
TCCAAAGAAAAAAGTAATAGCTGTAGAATATTAGTTCCTTCATATCGGCAGAAGAAAGATGACATGCTG

   420        430        440        450        460        470        480
ACACGTAAGATTCAGTCCTGGAAACTGGGAACTACCGTGCCTCCCATCAGTTTCACNCCTGGCCCCTGC

    490        500        510        520        530        540        550
AGTGAGGCTGACTTGAAGAGATGGGAGGCCATCCGGGAGGCCAGCAGACTCAGGCACAAGAAAAGGCTG

     560        570        580        590        600        610        620
ATGGTGGAGAGACTCTTTCAAAAGATTTATGGTGAGAATGGGAGTAAGTCCATGAGTGATGTCAGCGCA

      630        640        650        660        670        680        690
GAAGATGTTCAAAACTTGCGTCAGCTGCGTTACGAGGAGATGCAGAAAATAAAATCACAATTAAAAGAA

       700        710        720        730        740        750
CAAGATCAGAAATGGCAGGATGACCTTGCAAAATGGAAAGATCGTCGAAAAAGTTACACTTCAGATCTG

760
CAGAAG
```

FIG.28B

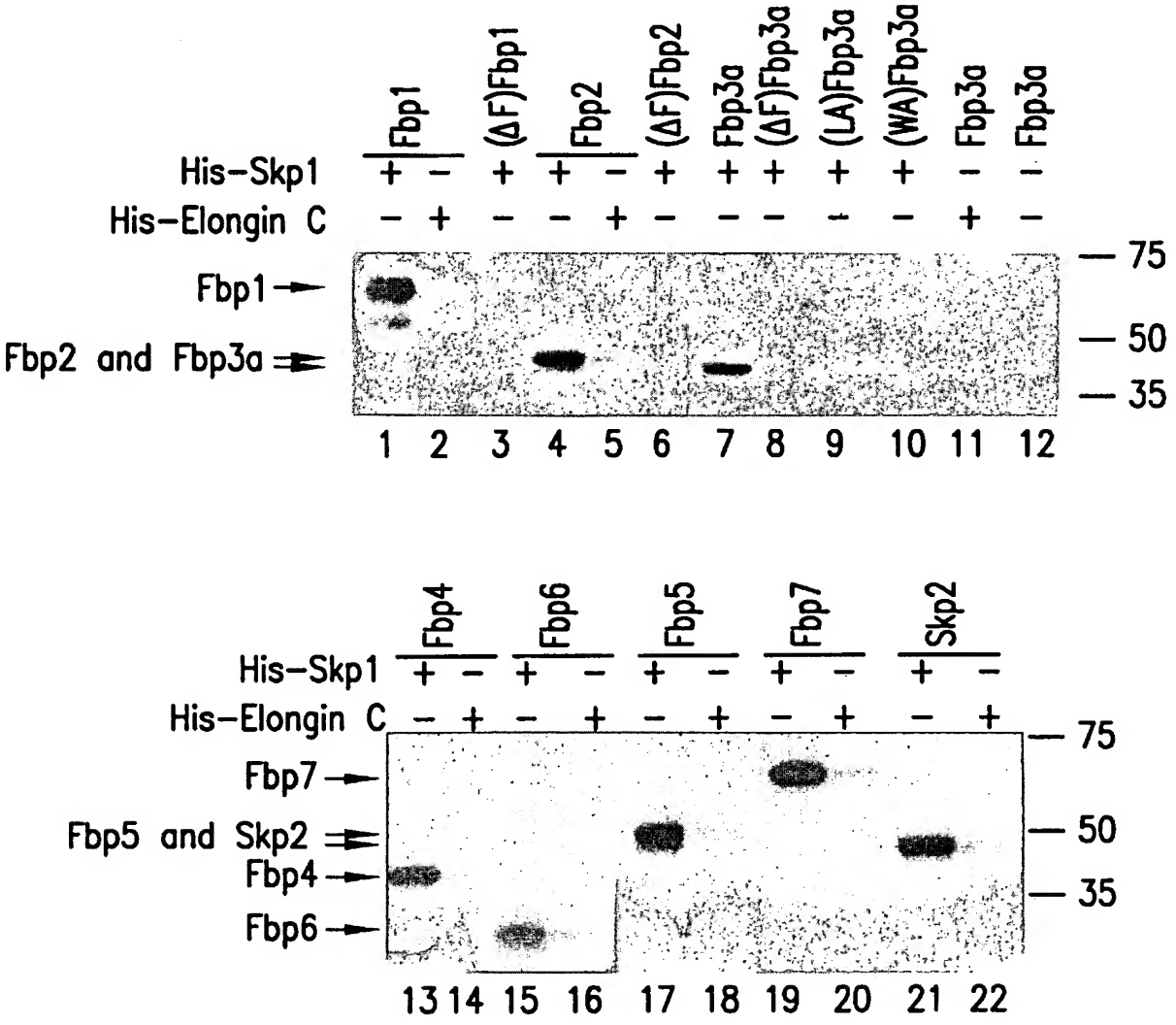

Fbp1
(ΔF)Fbp1
Fbp2
(ΔF)Fbp2
Fbp3α
(ΔF)Fbp3α
(LA)Fbp3α
(WA)Fbp3α
Fbp3α
Fbp3α
His-Skp1
His-Elongin C
Fbp1
Fbp2 and Fbp3α
75
50
35
1 2 3 4 5 6 7 8 9 10 11 12
Fbp4
Fbp6
Fbp5
Fbp7
Skp2
His-Skp1
His-Elongin C
Fbp7
Fbp5 and Skp2
Fbp4
Fbp6
75
50
35
13 14 15 16 17 18 19 20 21 22

FIG.29

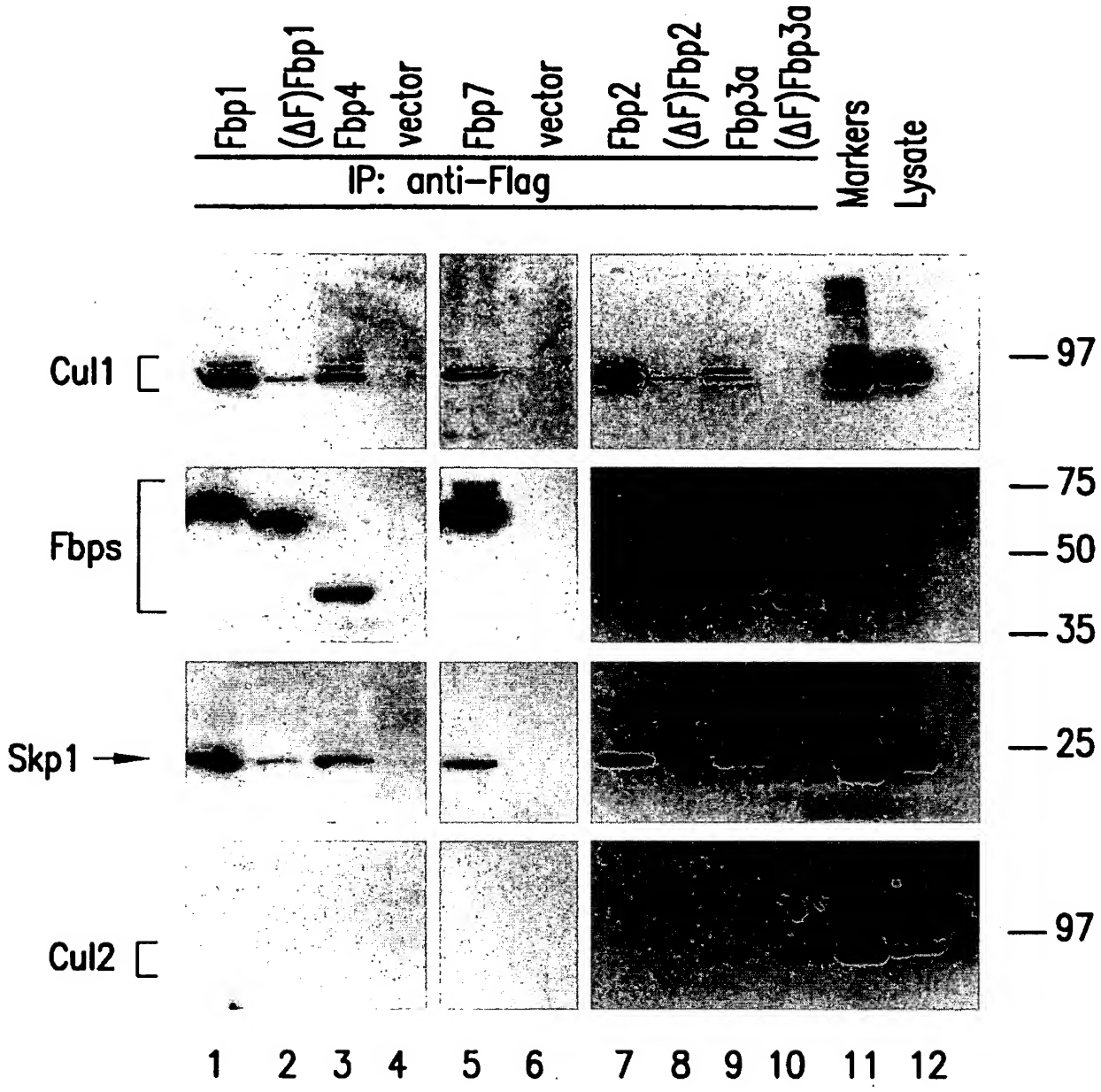

Fbp1
(ΔF)Fbp1
Fbp4
vector
Fbp7
vector
Fbp2
(ΔF)Fbp2
Fbp3a
(ΔF)Fbp3a
Markers
Lysate
IP: anti-Flag
Cul1
Fbps
Skp1
Cul2
97
75
50
35
25
97
1 2 3 4 5 6 7 8 9 10 11 12

FIG.30

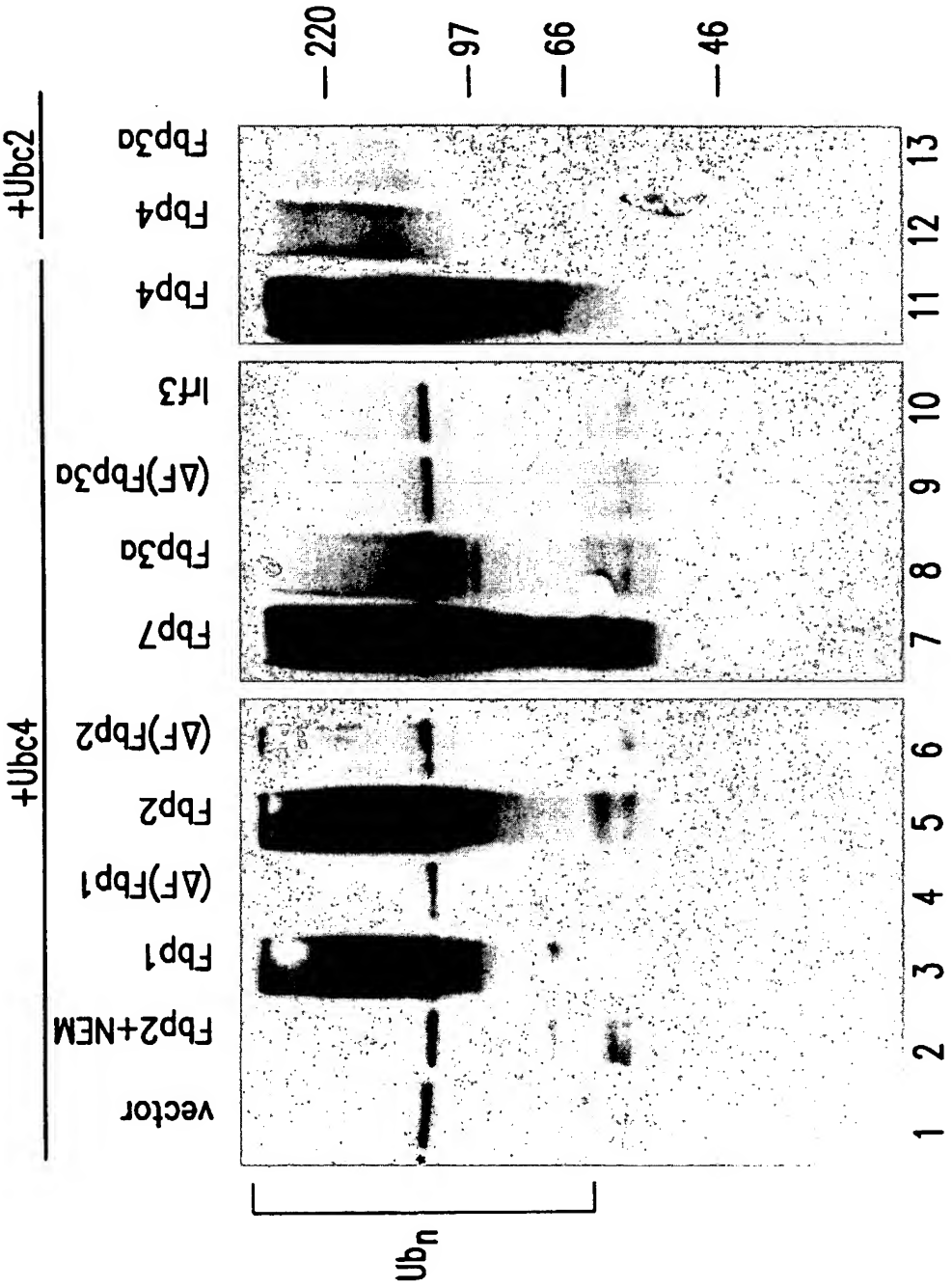

220
97
66
46
+Ubc2
Fbp3α
Fbp4
Fbp4
+Ubc4
Irf3
(ΔF)Fbp3α
Fbp3α
Fbp7
(ΔF)Fbp2
Fbp2
(ΔF)Fbp1
Fbp1
Fbp2+NEM
vector
13
12
11
10
9
8
7
6
5
4
3
2
1
Ubn

FIG.31

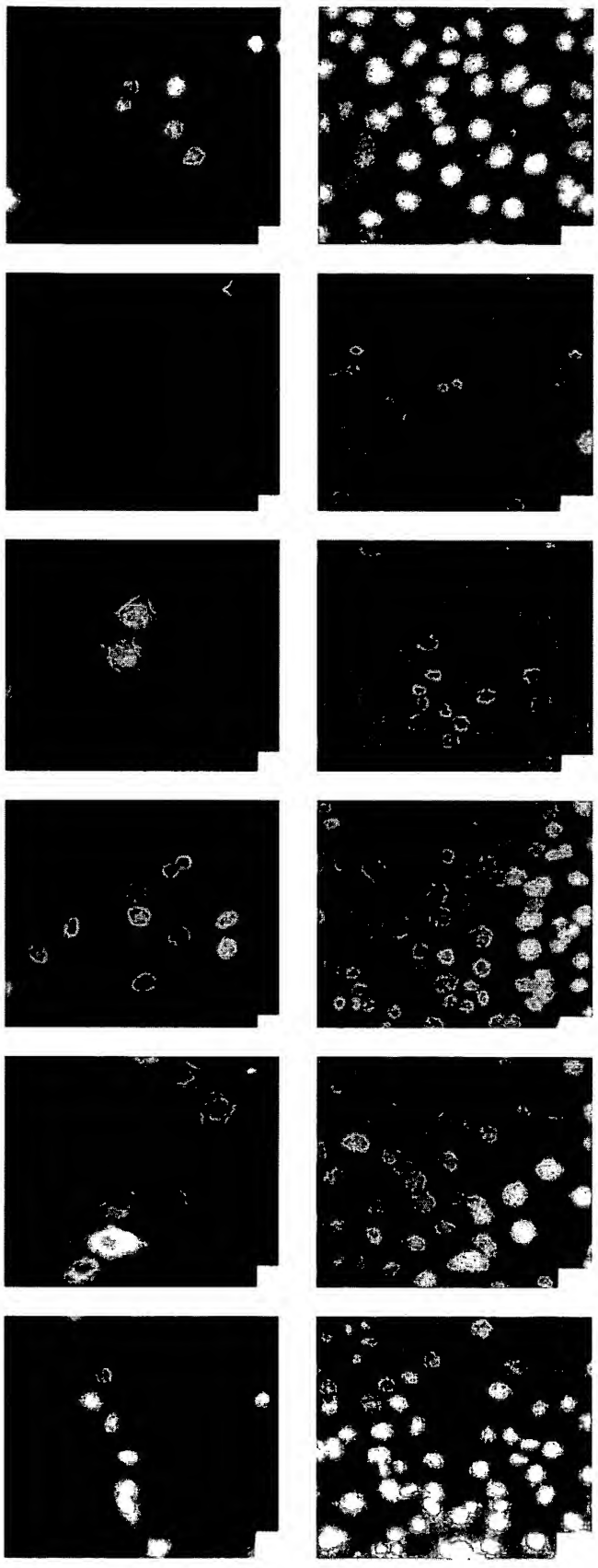
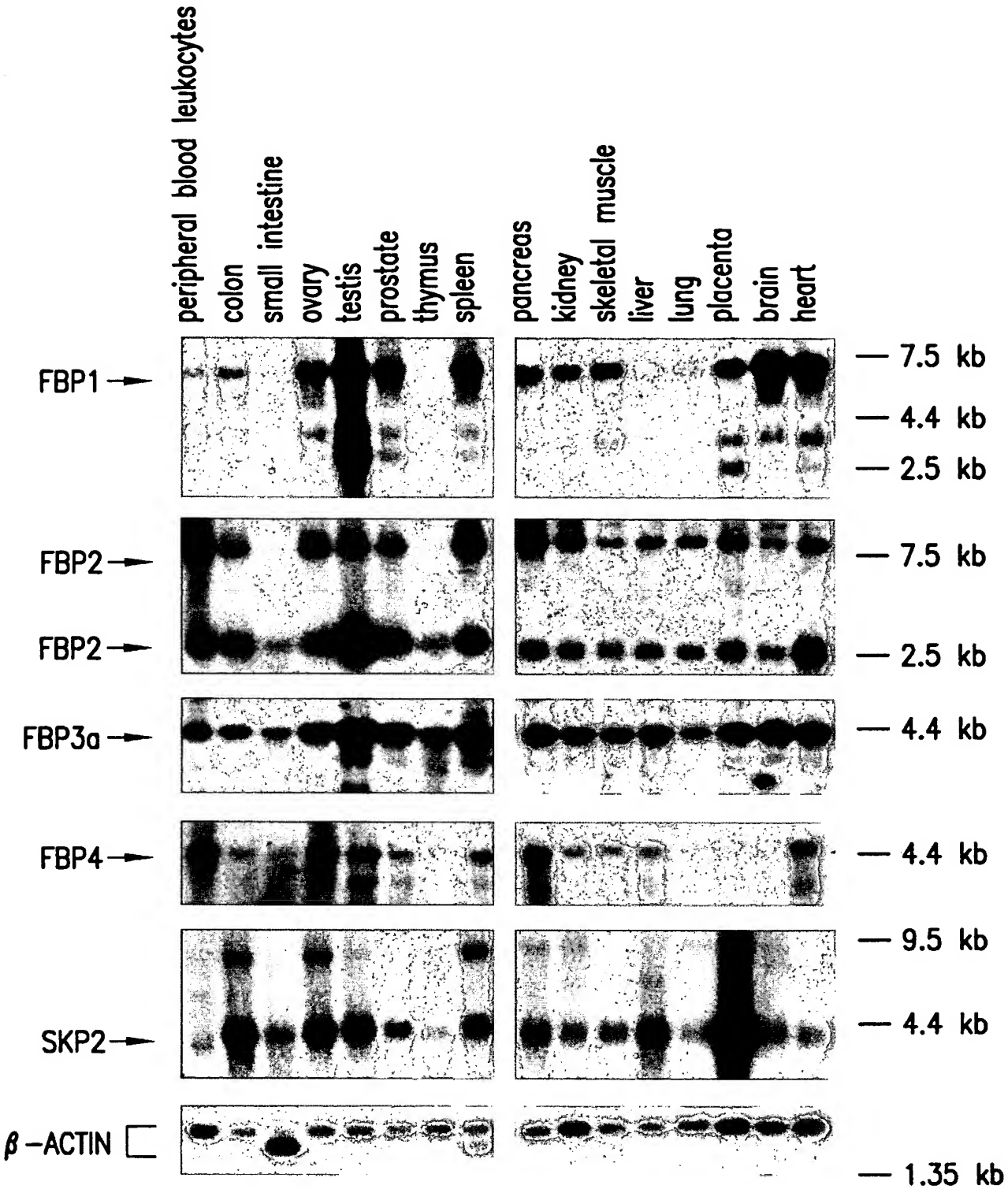


FIG.32A FIG.32B FIG.32C FIG.32D FIG.32E FIG.32F FIG.32G FIG.32H FIG.32I FIG.32J FIG.32K FIG.32L


peripheral blood leukocytes
colon
small intestine
ovary
testis
prostate
thymus
spleen
pancreas
kidney
skeletal muscle
liver
lung
placenta
brain
heart
FBP1
FBP2
FBP2
FBP3α
FBP4
SKP2
β-ACTIN
7.5 kb
4.4 kb
2.5 kb
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4.4 kb
9.5 kb
4.4 kb
1.35 kb

FIG.33

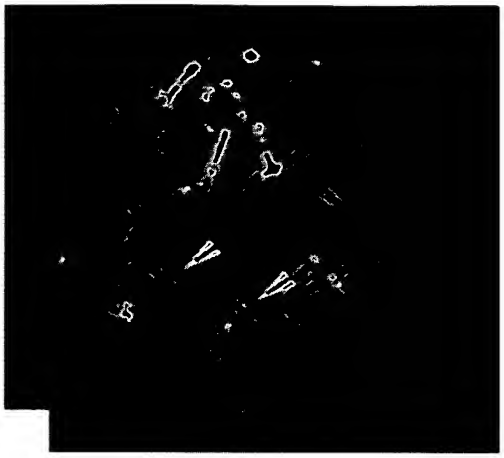


FIG.34A

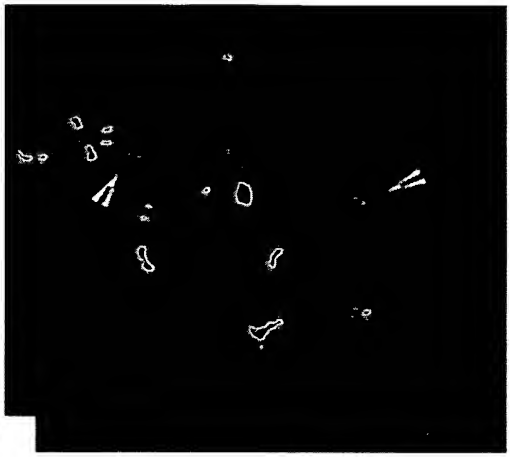


FIG.34B

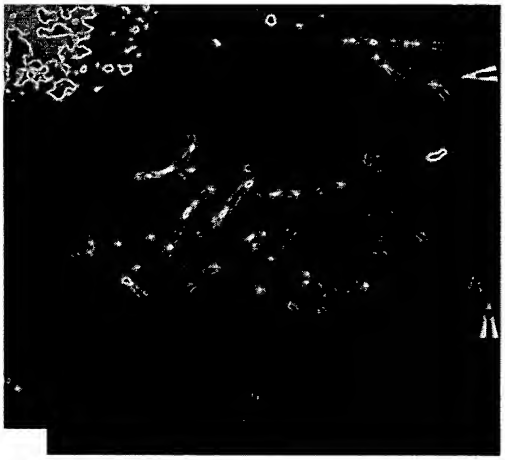


FIG.34C

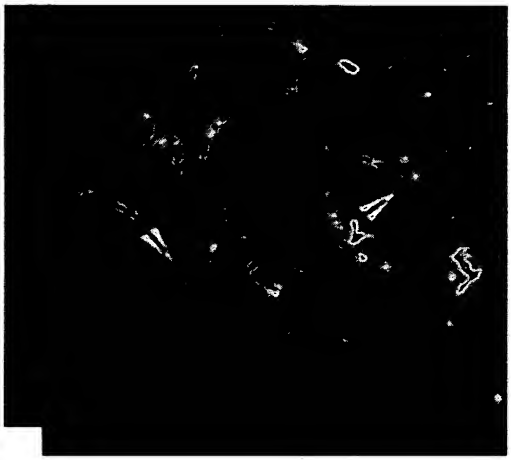
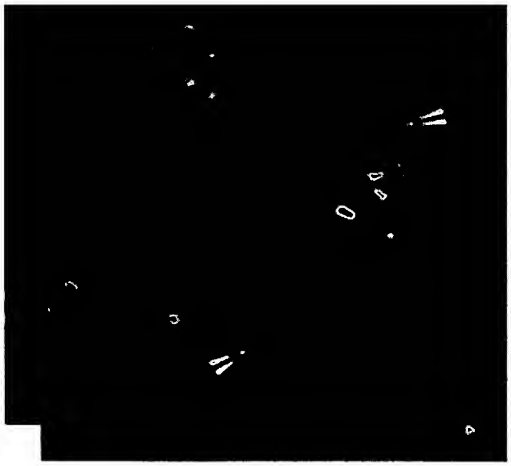


FIG.34D

FIG.34E



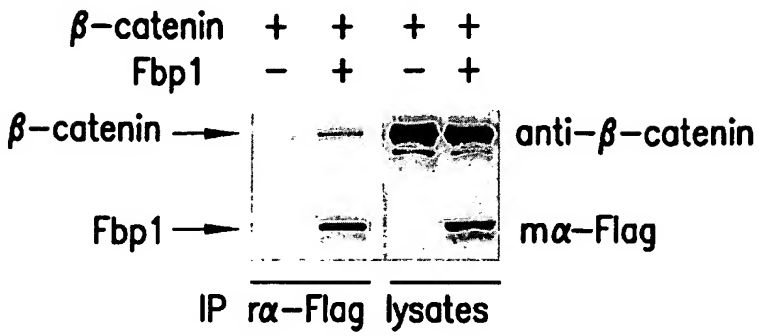


FIG.35A

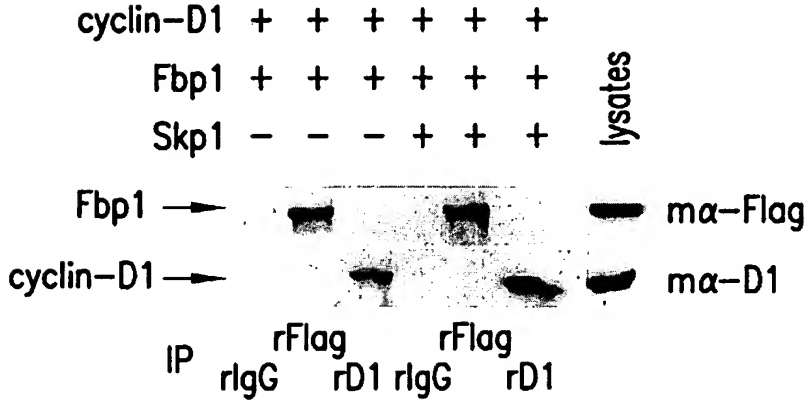


FIG.35B

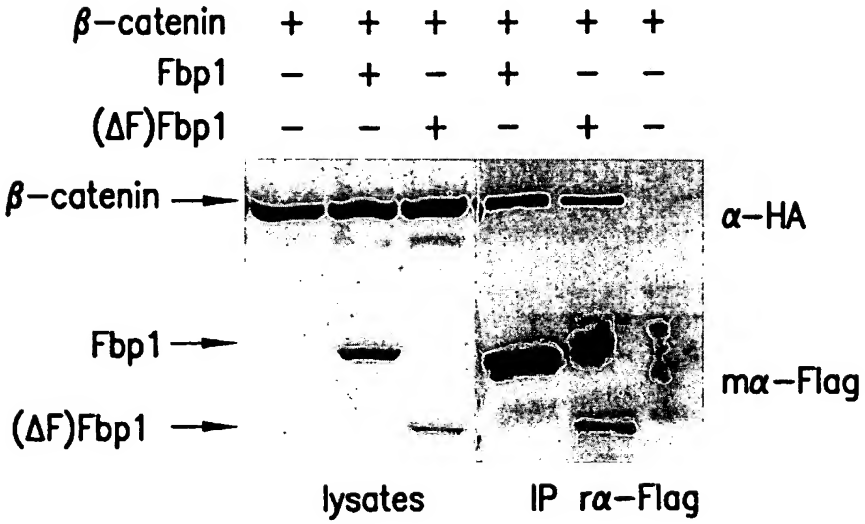


FIG.35C

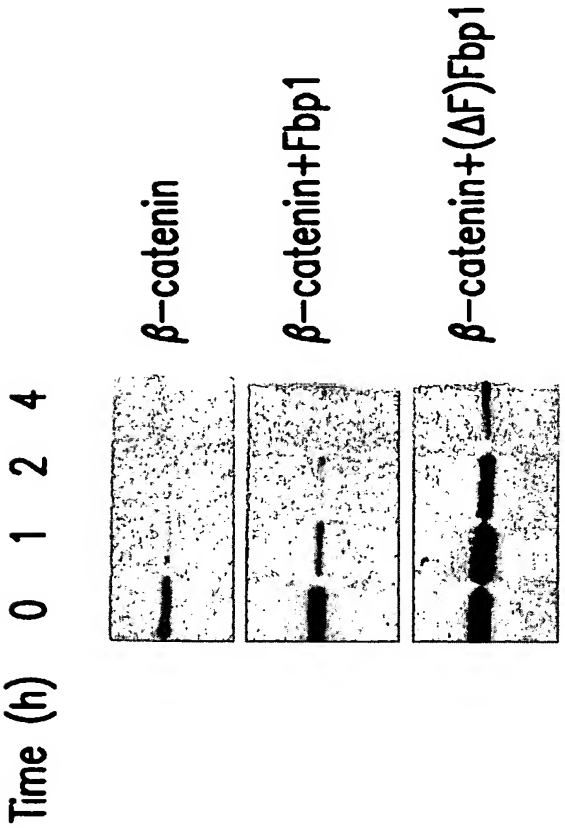


FIG.36B

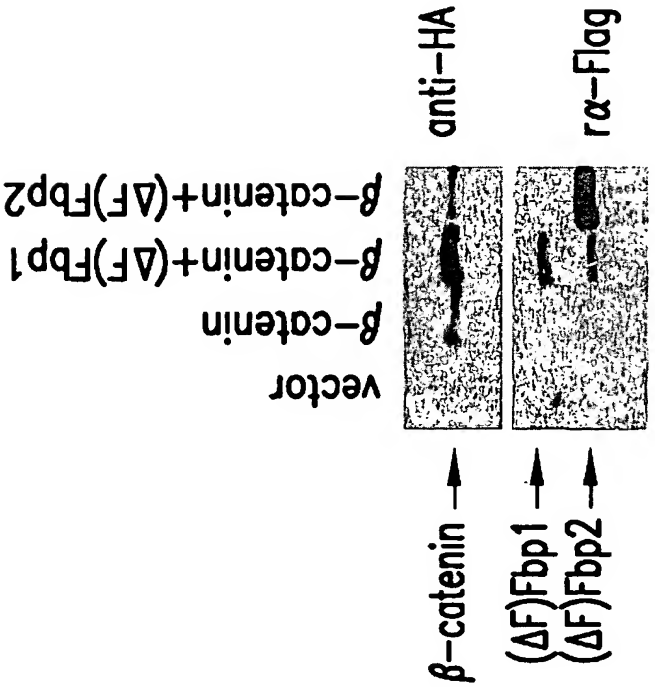


FIG.36A

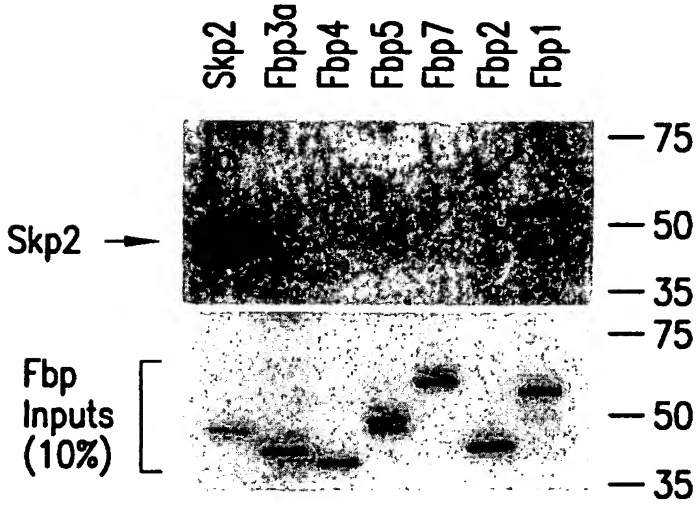


FIG.37A

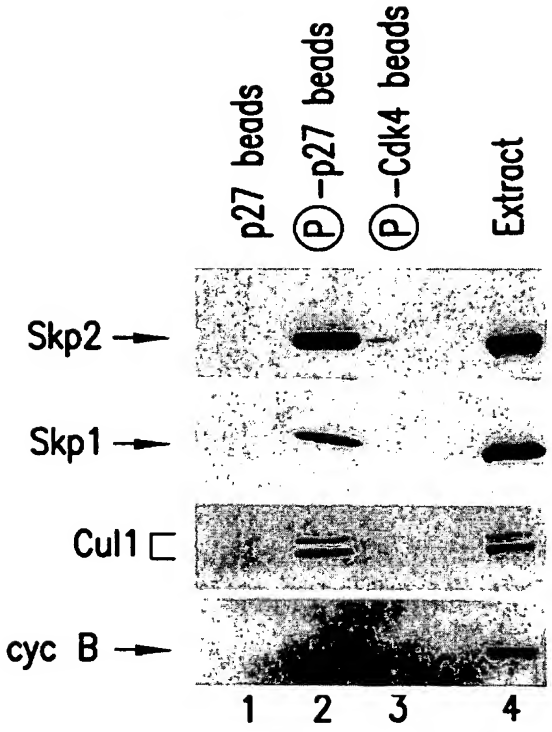


FIG.37B

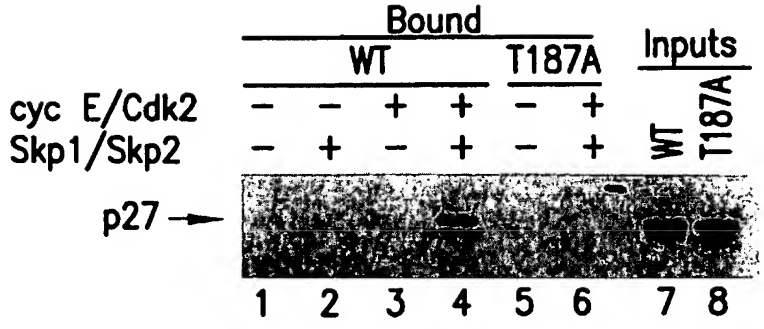


FIG.37C

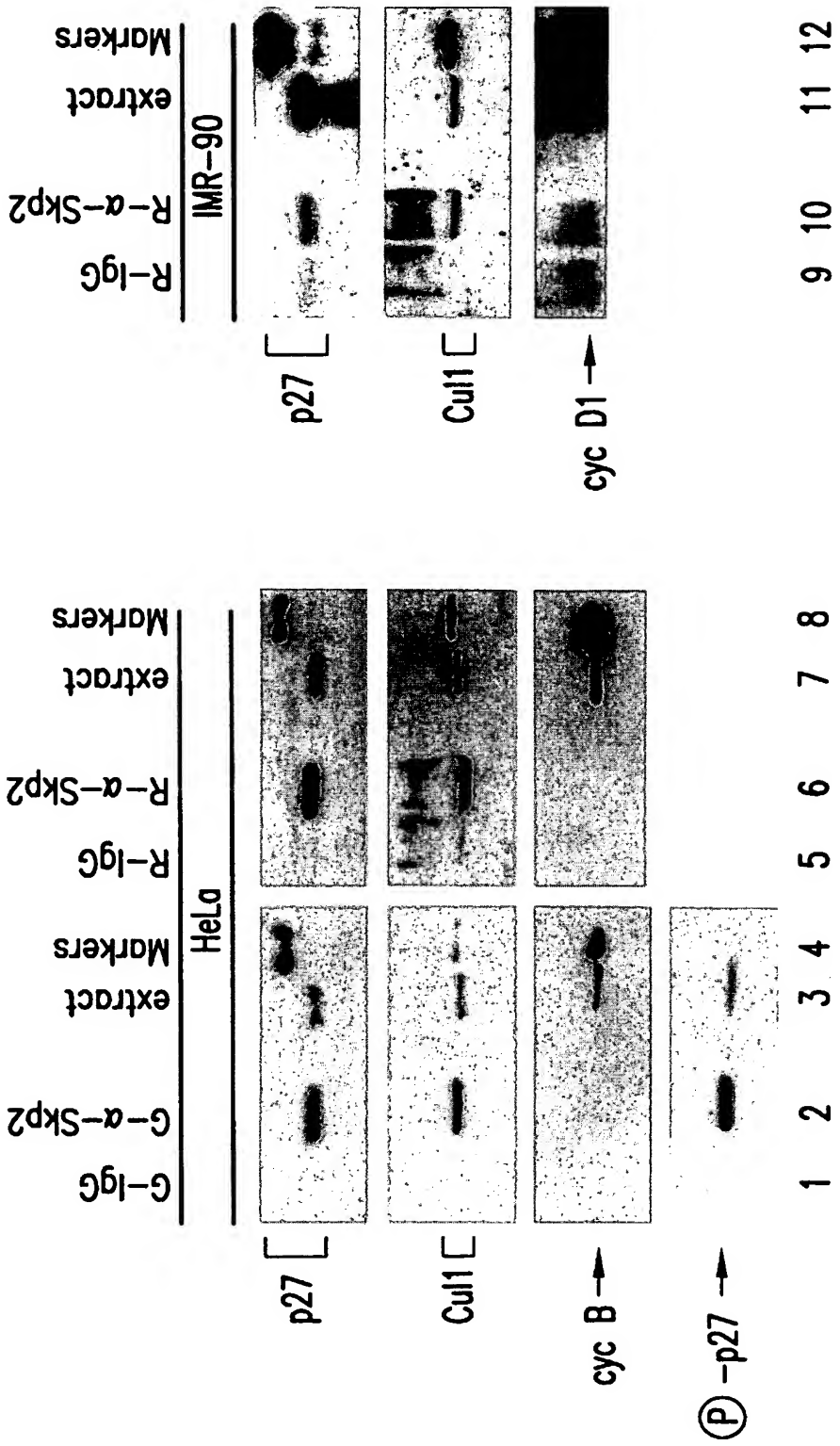

IMR-90
R-IgG
R-α-Skp2
extract
Markers
HeLa
G-IgG
G-α-Skp2
extract
Markers
R-IgG
R-α-Skp2
extract
Markers
p27
Cul1
cyc D1
cyc B
Ⓟ-p27
1 2 3 4 5 6 7 8 9 10 11 12

FIG.38

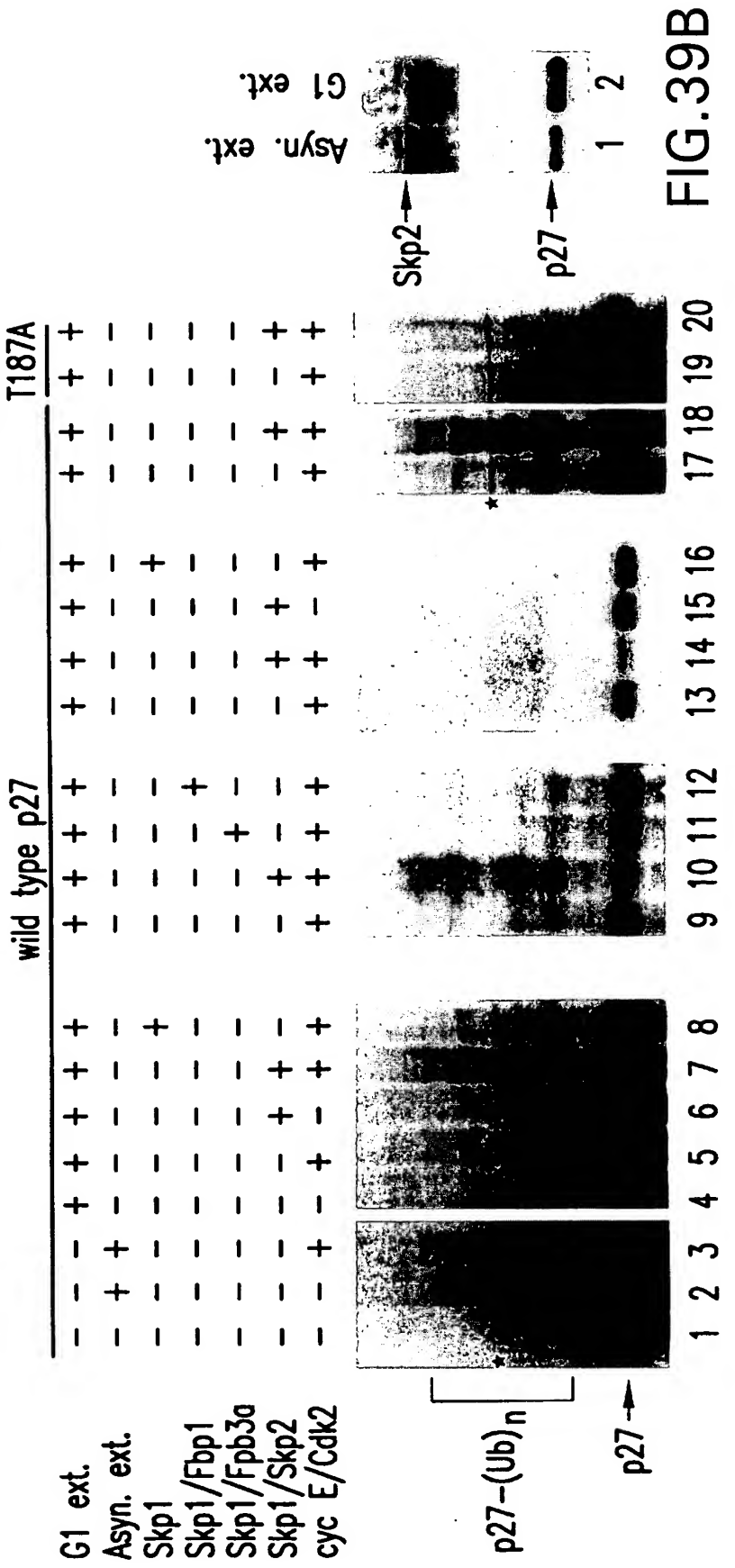


FIG.39A

FIG.39B

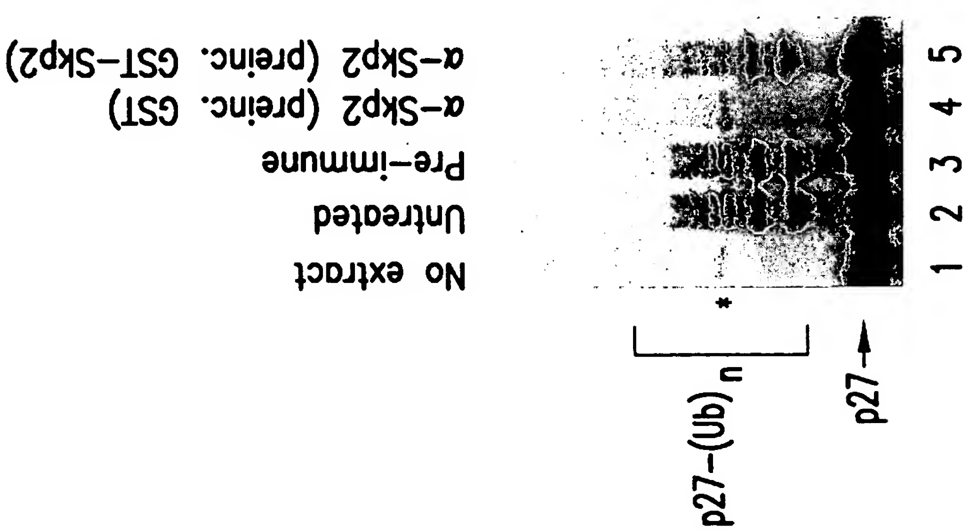


FIG.40A

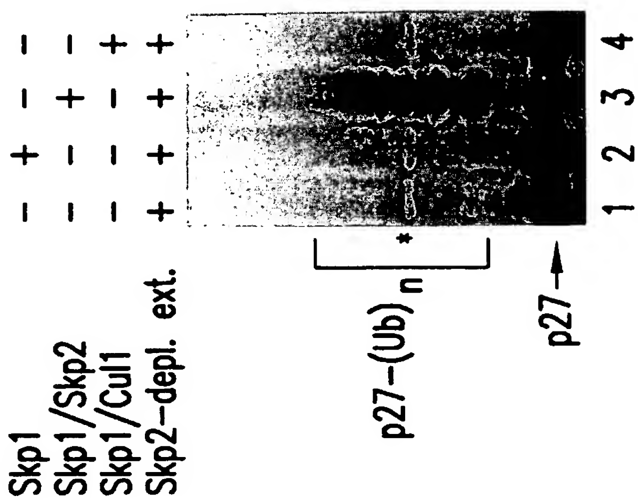


FIG.40B

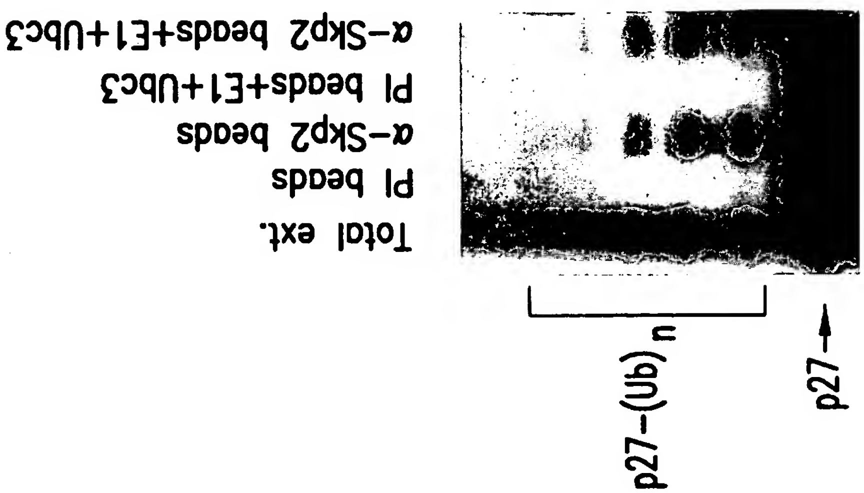


FIG.40C

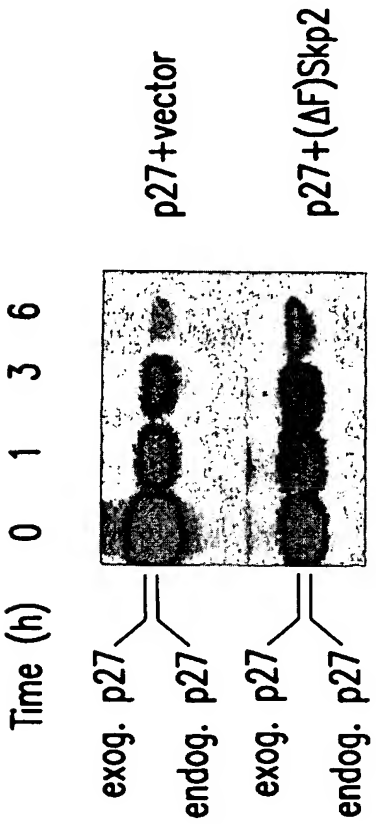


FIG.41B

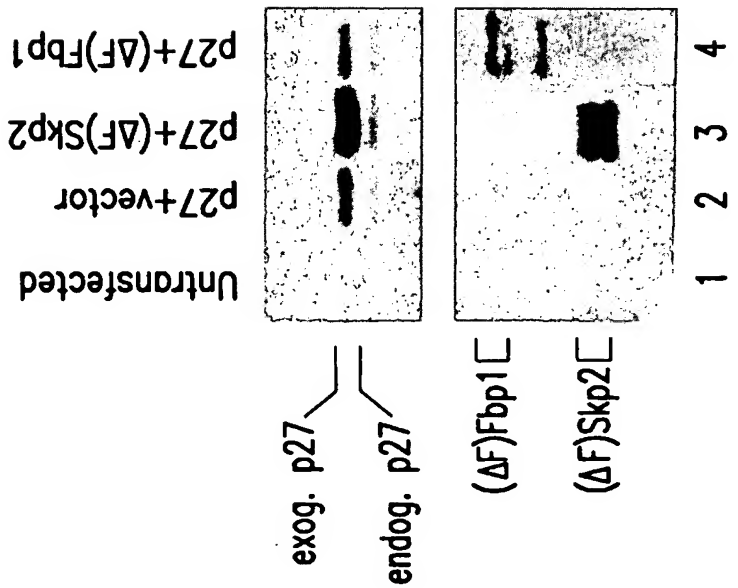


FIG.41A

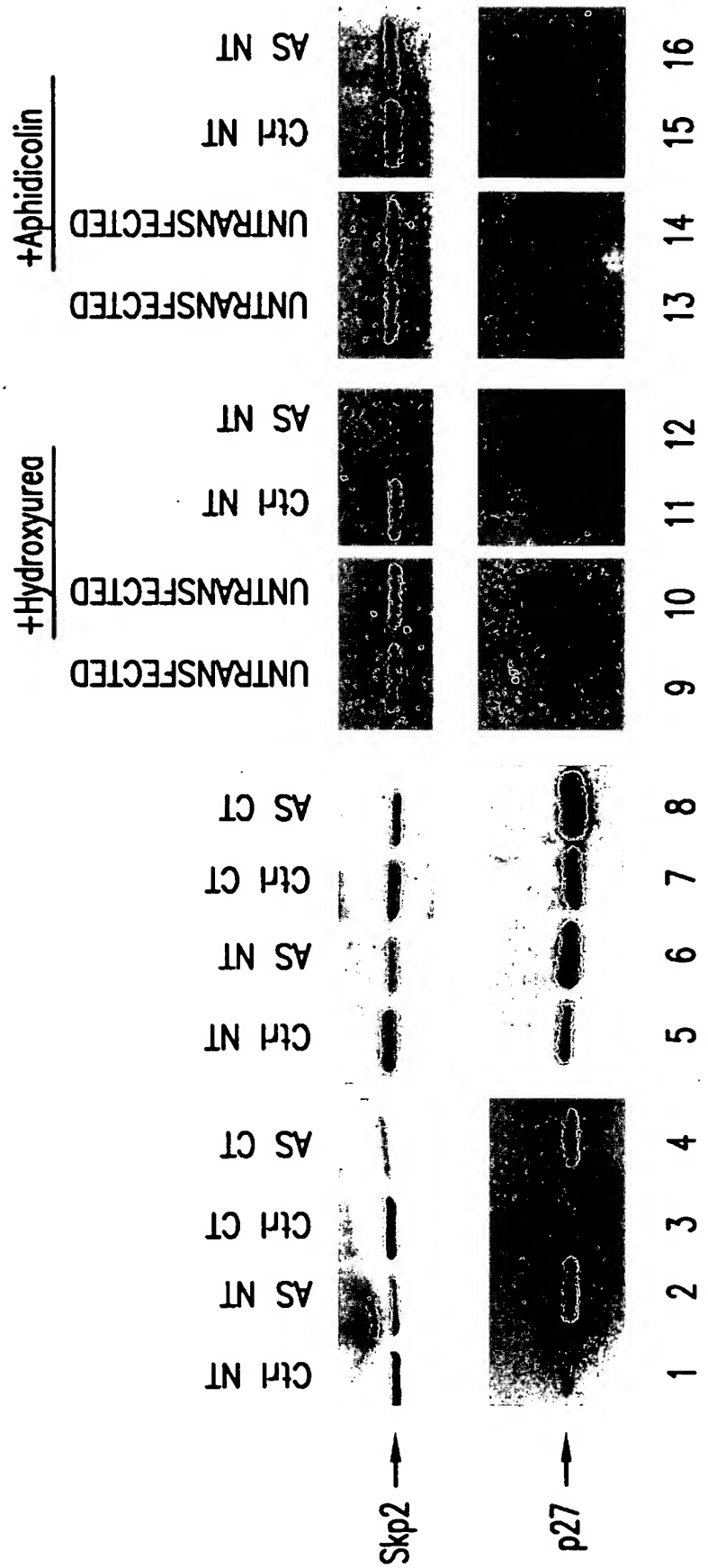

+Aphidicolin
+Hydroxyurea
Ctrl NT
AS NT
UNTRANSFECTED
Ctrl CT
AS CT
Skp2
p27
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

FIG.42

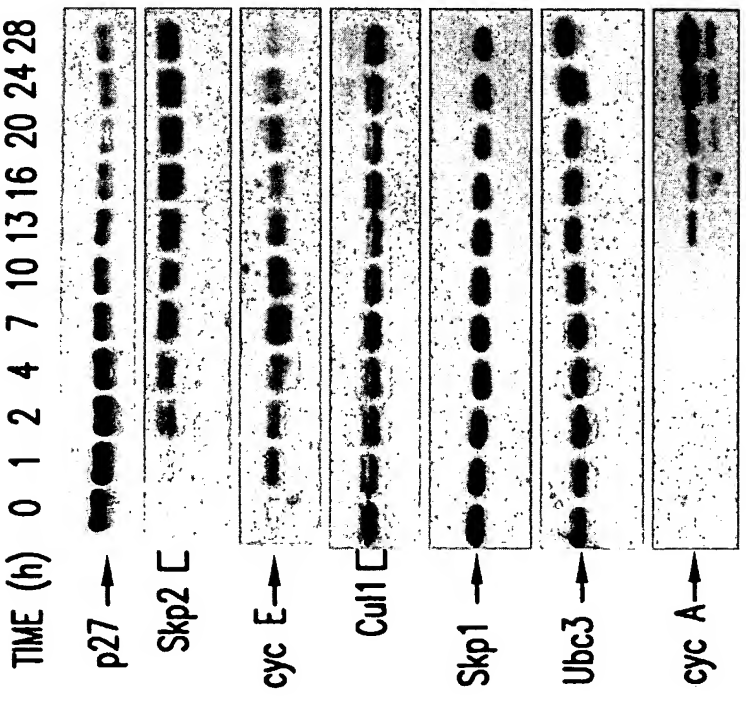


FIG.43A

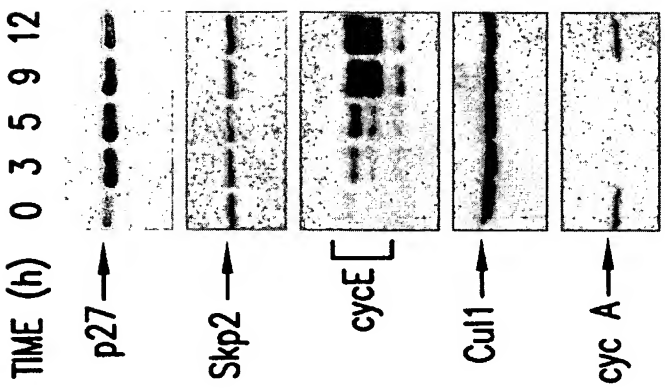


FIG.43B

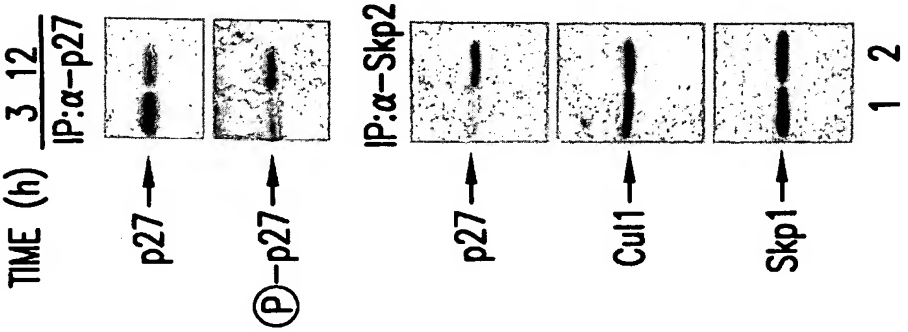


FIG.43C

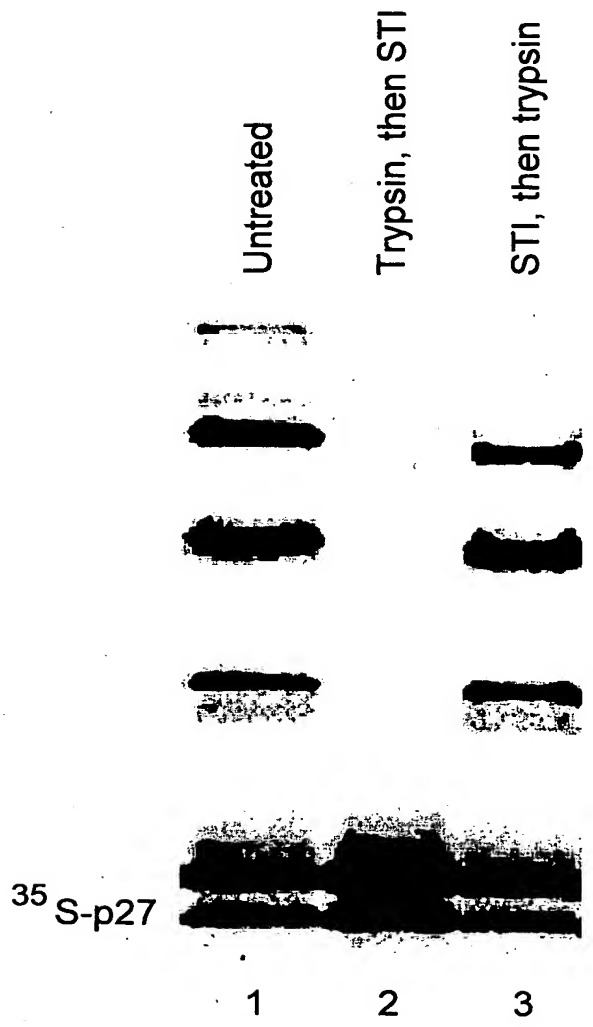


FIG.44

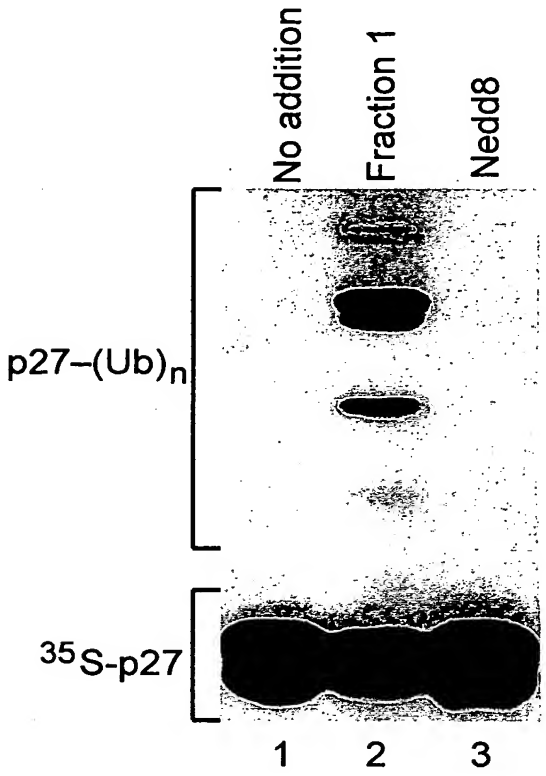


FIG.45A

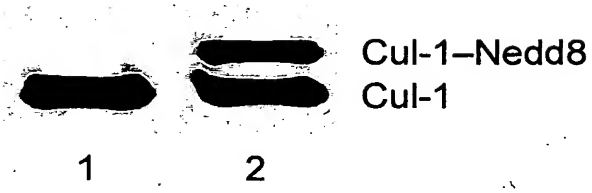


FIG.45B

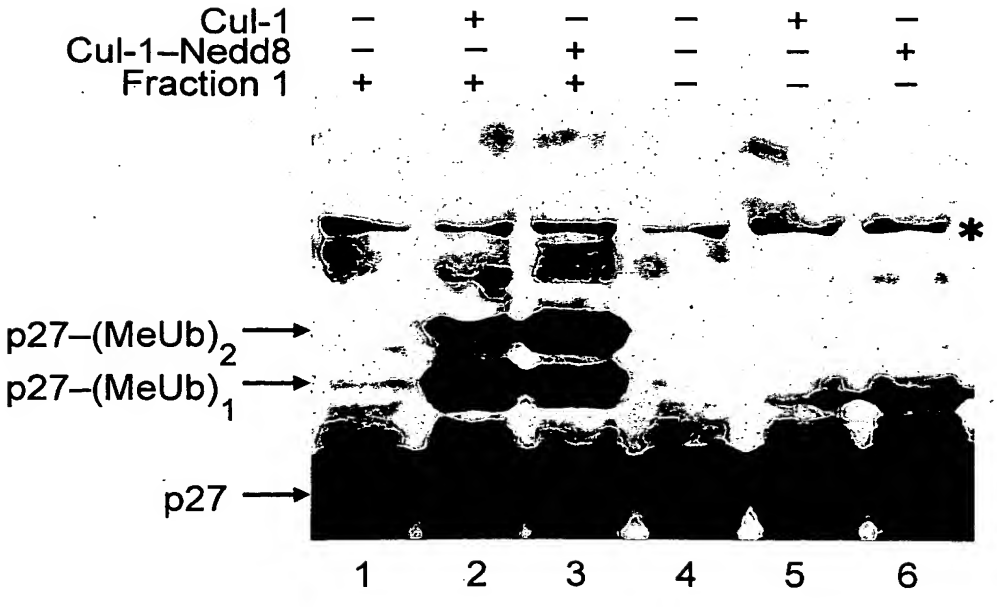


FIG.45C

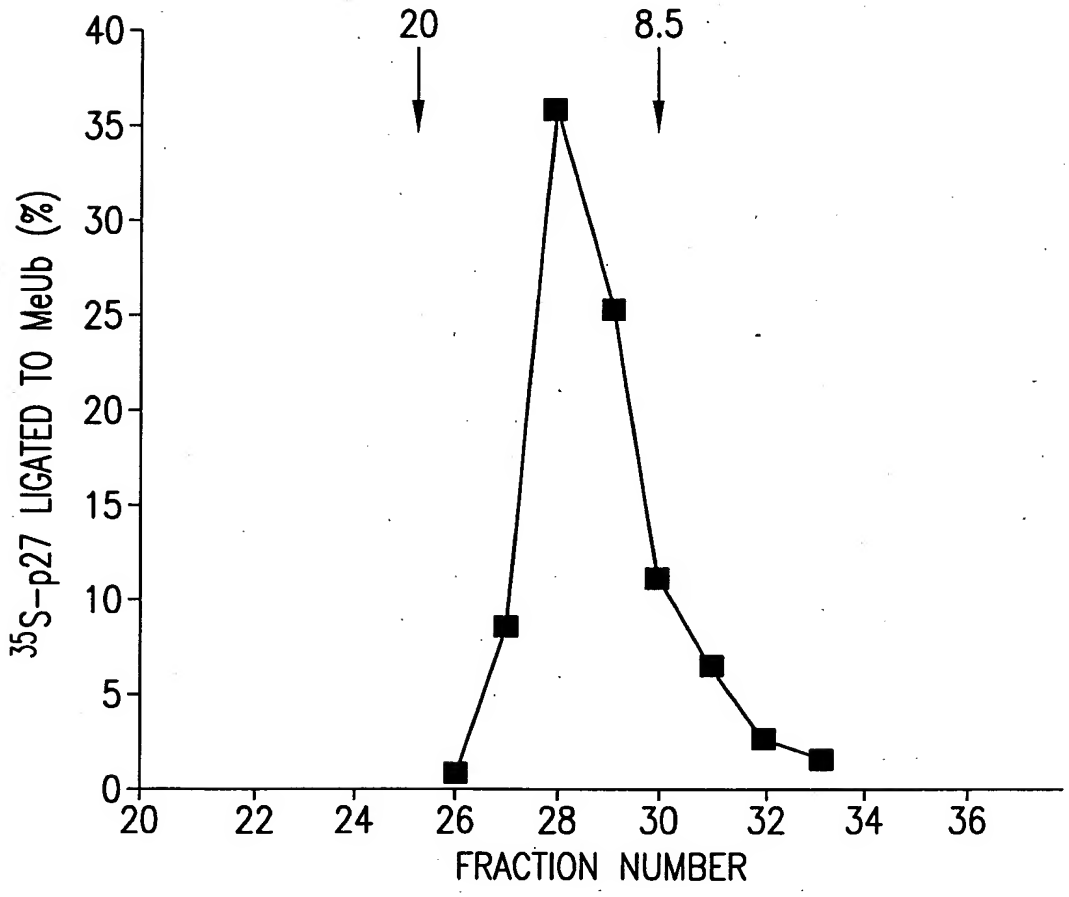

20
8.5
40
35
30
25
20
15
10
5
0
^{35}S-p27 LIGATED TO MeUb (%)
20
22
24
26
28
30
32
34
36
FRACTION NUMBER

FIG.46A

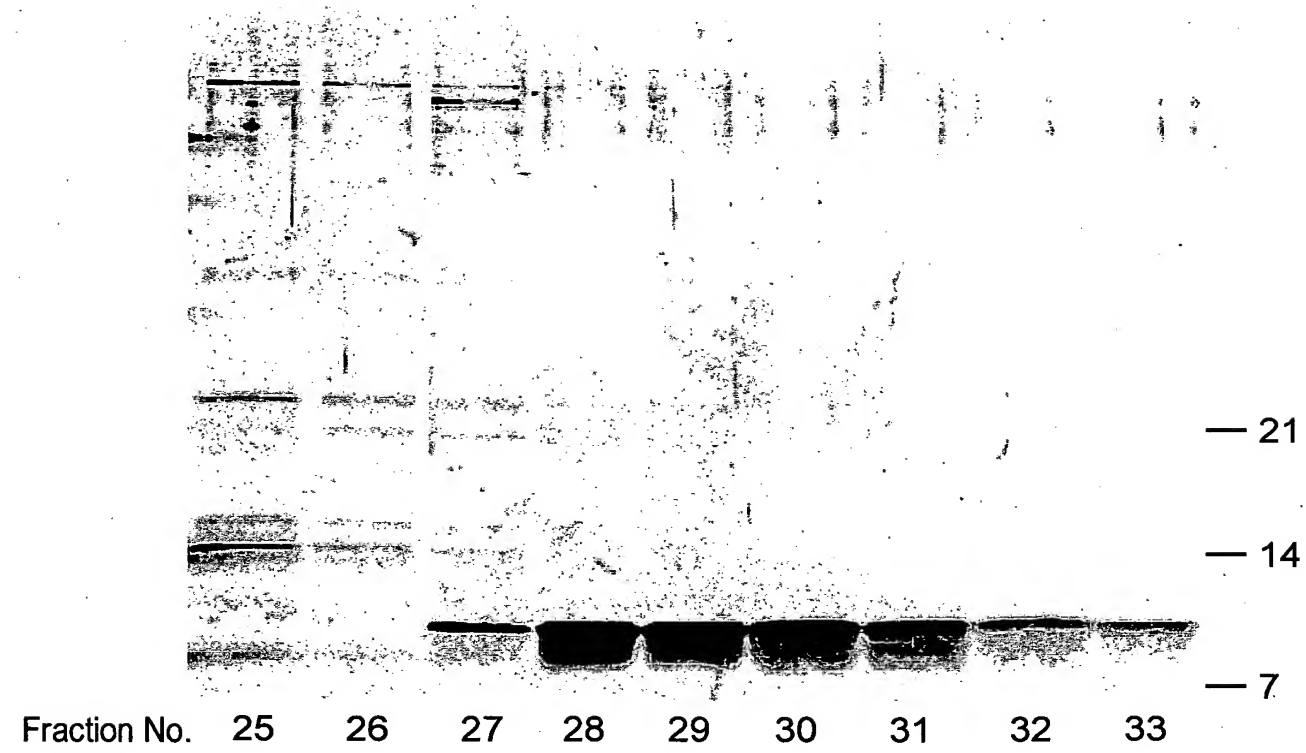


FIG.46B

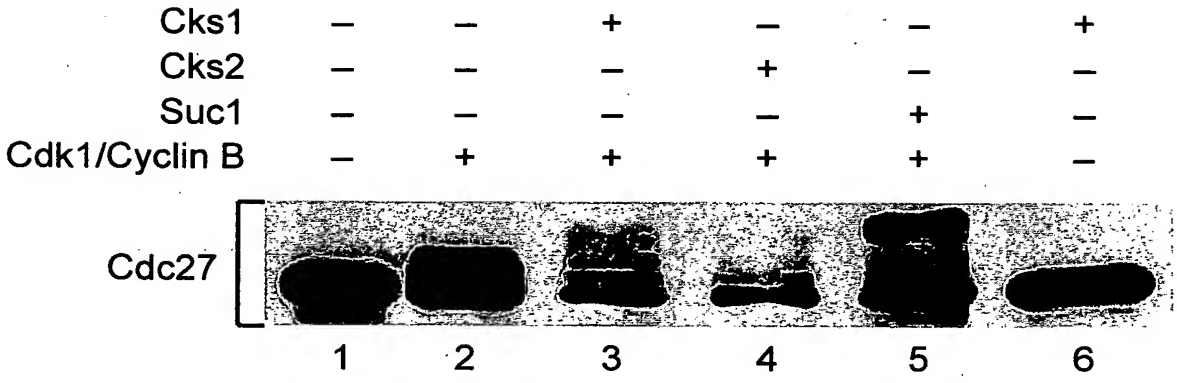


FIG.47

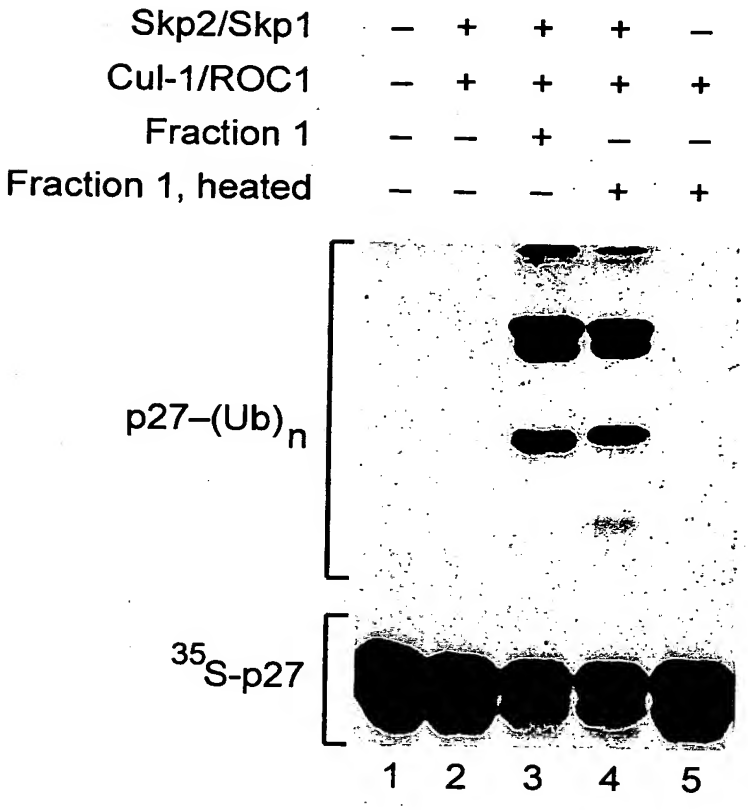

Skp2/Skp1 – + + + –
Cul-1/ROC1 – + + + +
Fraction 1 – – + – –
Fraction 1, heated – – – + +
p27–(Ub)n
35S-p27
1 2 3 4 5

FIG.48A

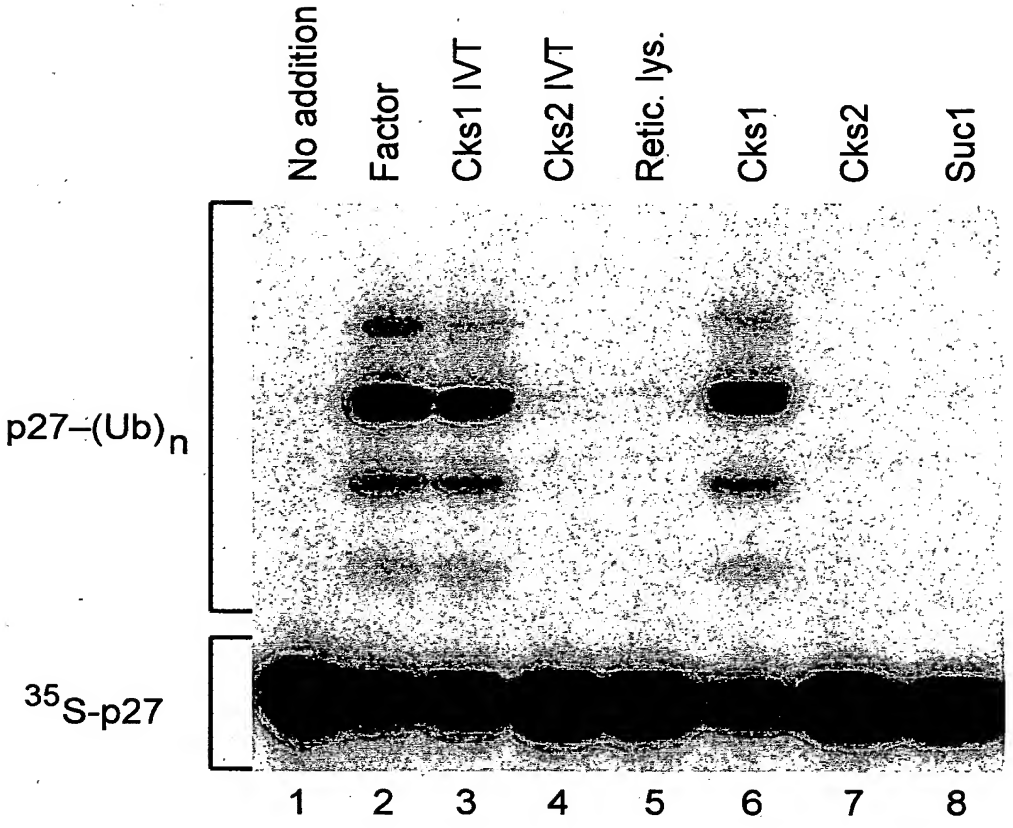

No addition
Factor
Cks1 IVT
Cks2 IVT
Retic. lys.
Cks1
Cks2
Suc1
p27–(Ub)n
35S-p27
1
2
3
4
5
6
7
8

FIG.48B

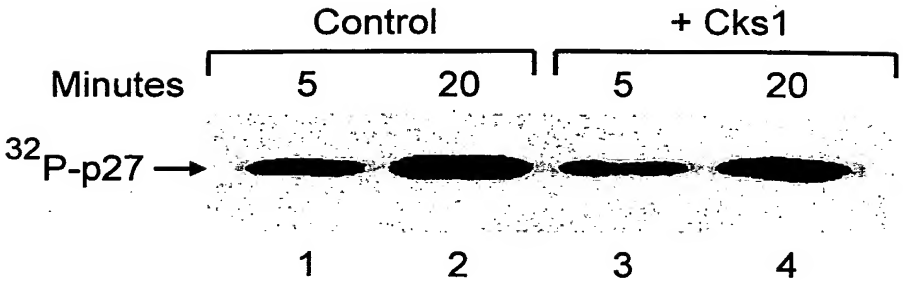


FIG.49A

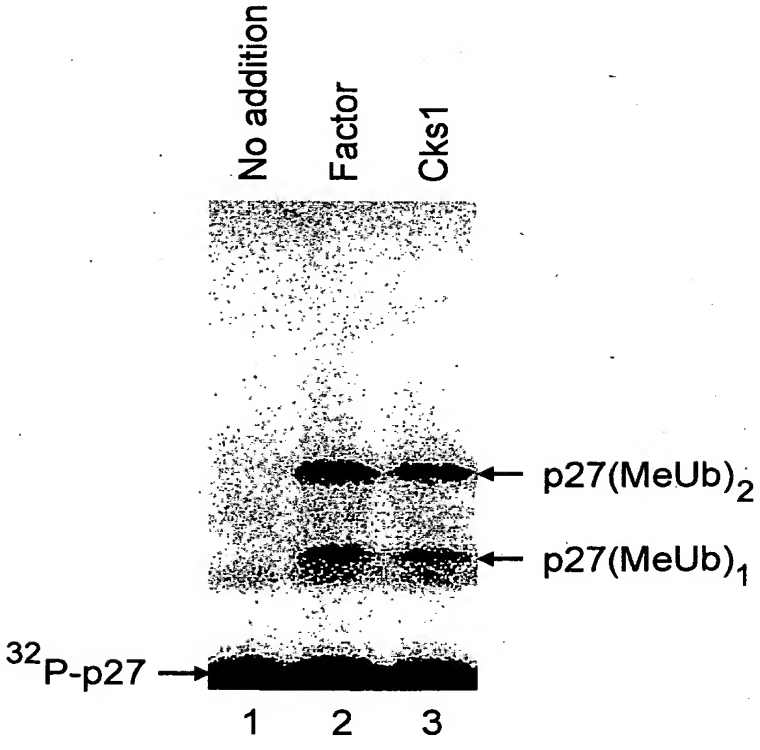


FIG.49B

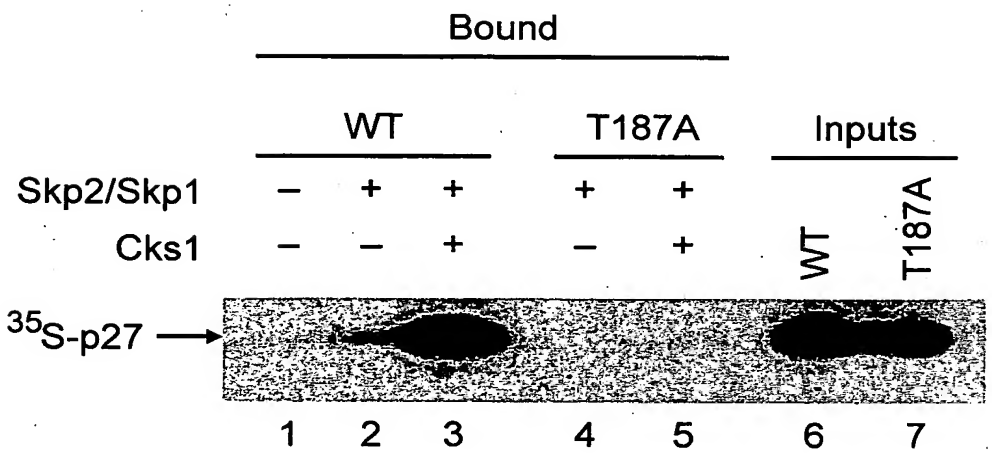


FIG.49C

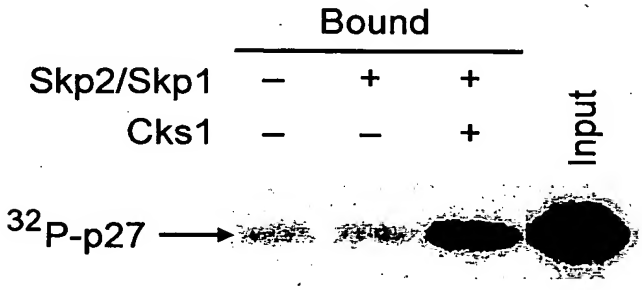


FIG.49D

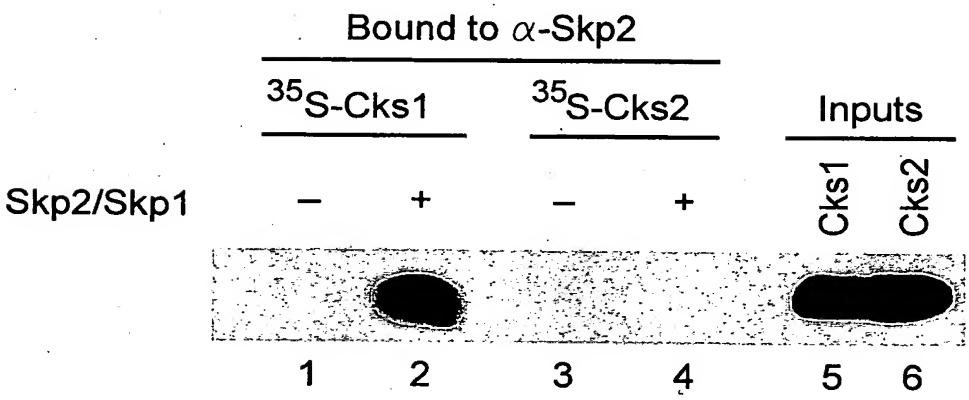


FIG.50A

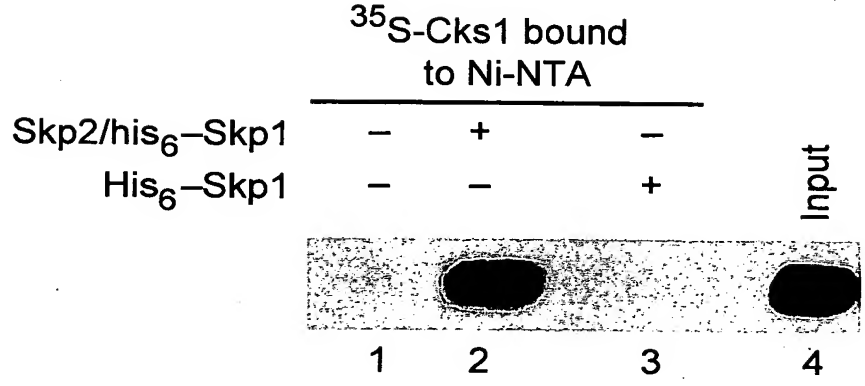


FIG.50B

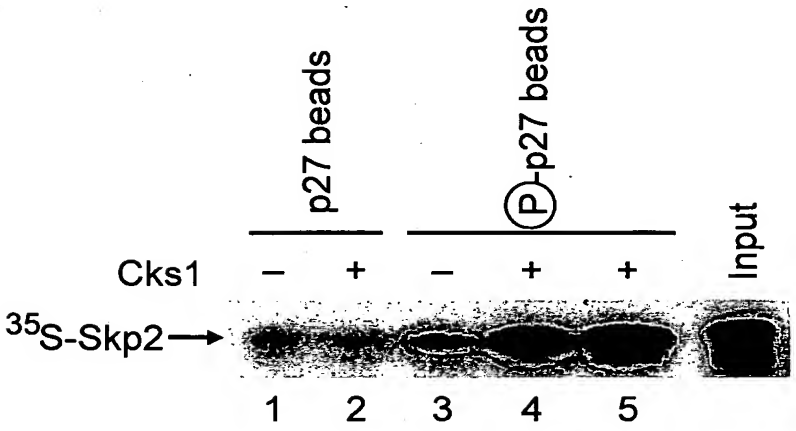


FIG.50C

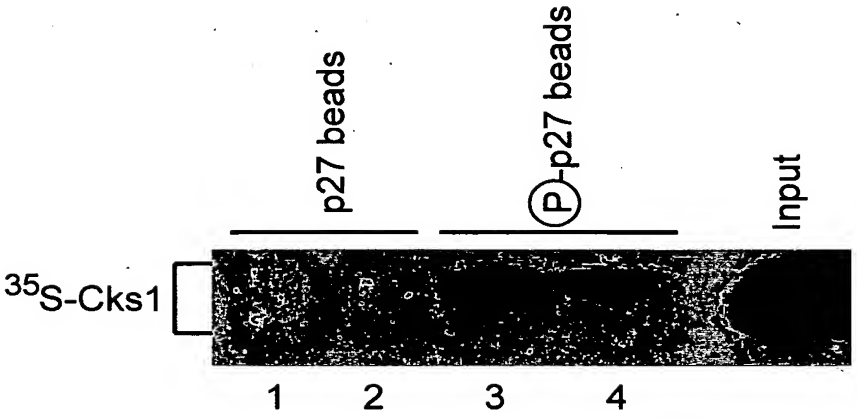


FIG.50D

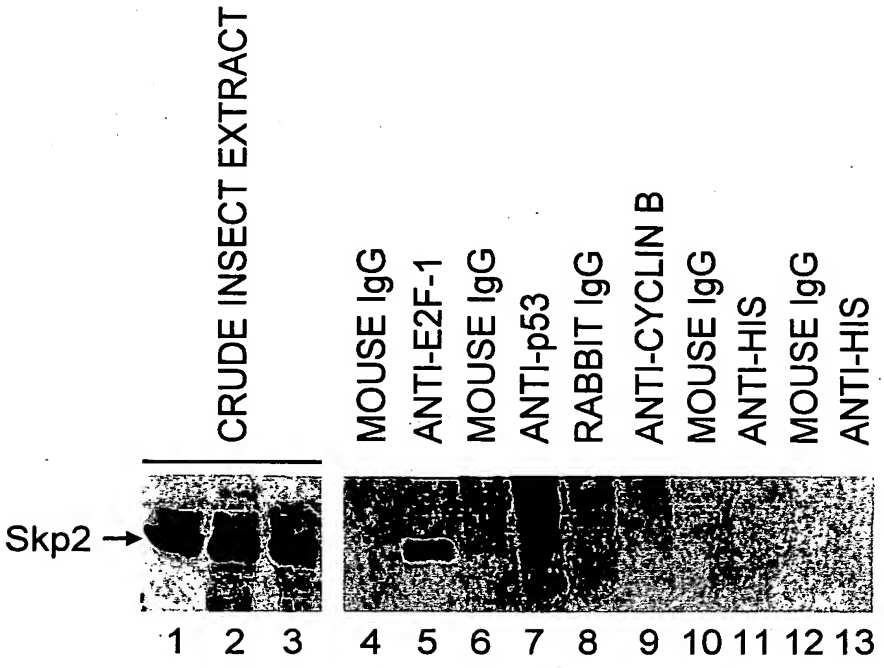


FIG.51A

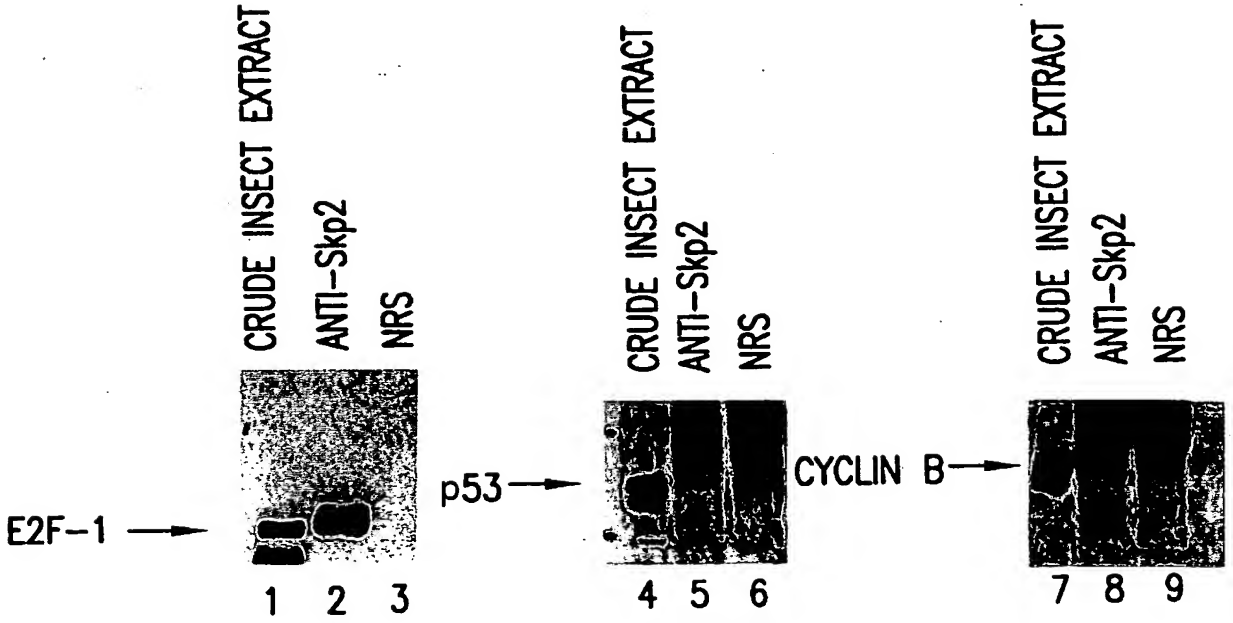


FIG.51B

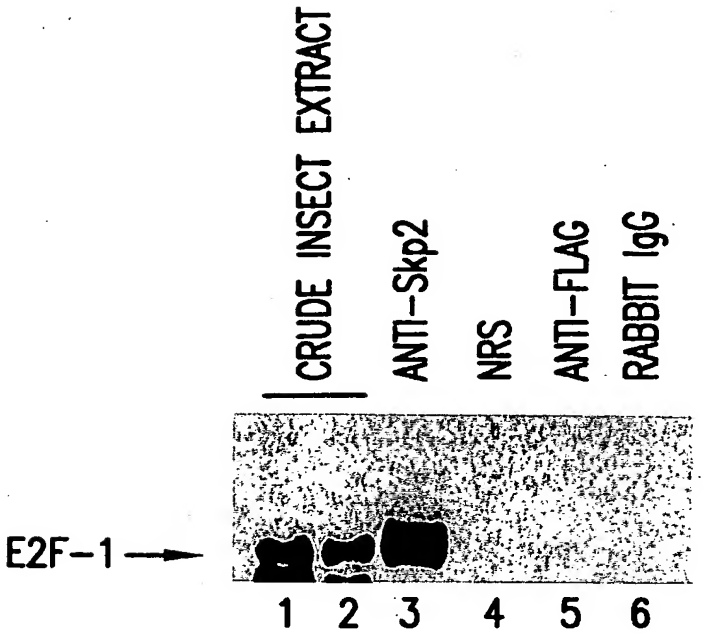

CRUDE INSECT EXTRACT
ANTI-Skp2
NRS
ANTI-FLAG
RABBIT IgG
E2F-1
1 2 3 4 5 6

FIG. 51C

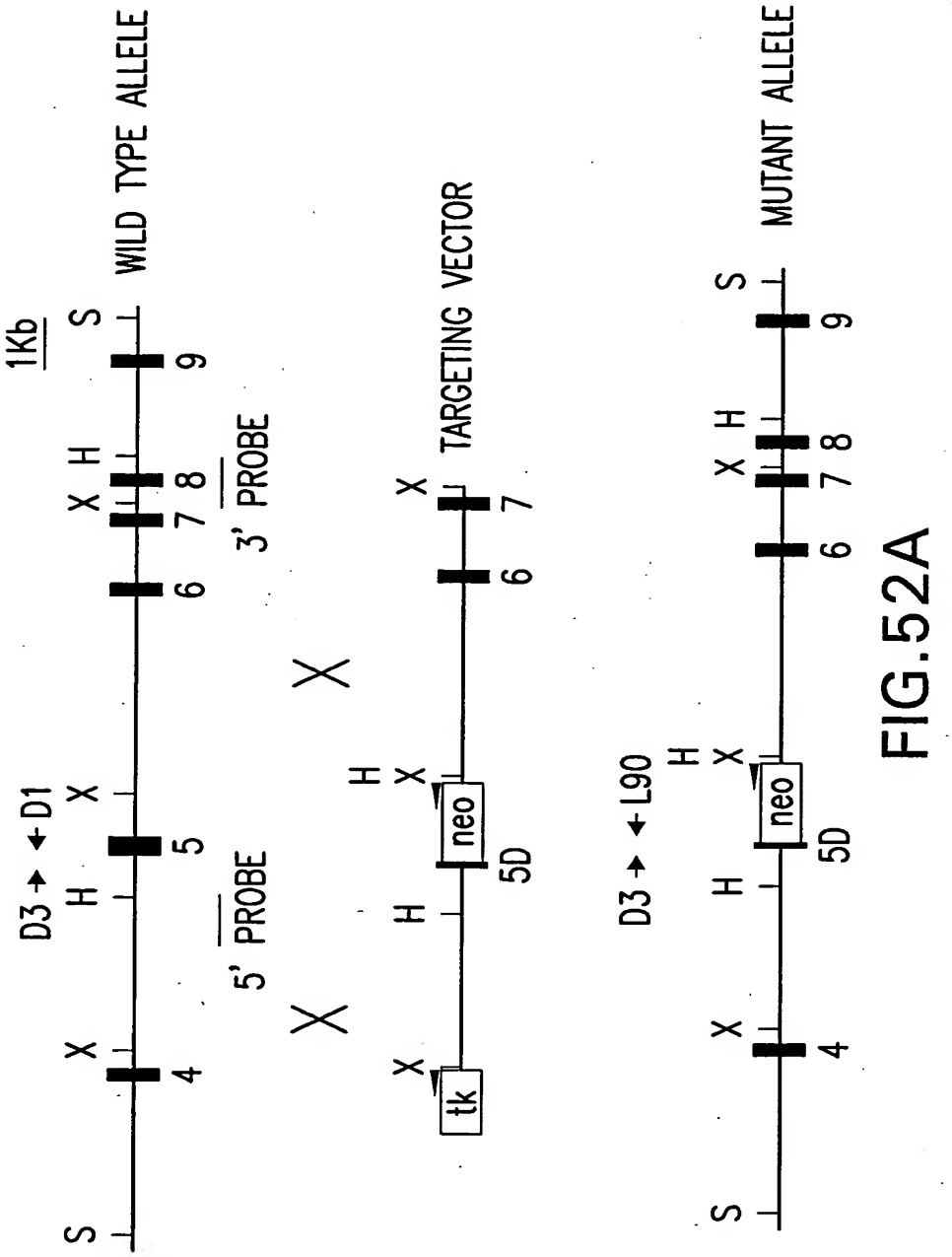

1Kb
WILD TYPE ALLELE
S
X H
9
7 8
6
3' PROBE
D3 → ← D1
X
5
H
X
4
5' PROBE
S
TARGETING VECTOR
X
7
6
H
X
neo
5D
H
X
tk
MUTANT ALLELE
S
X H
9
7 8
6
D3 → ← L90
H
X
neo
5D
H
X
4
S

FIG.52A

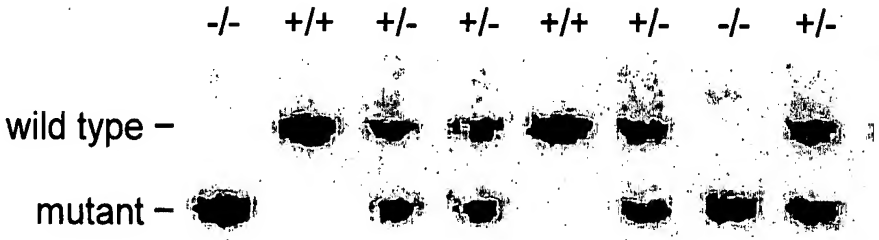


FIG.52B

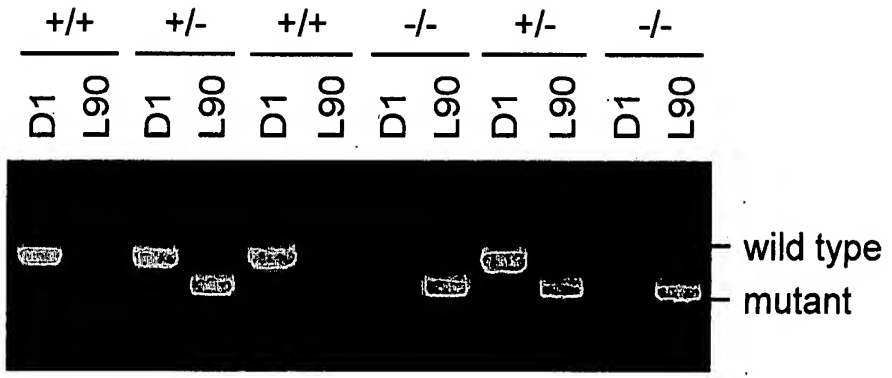


FIG.52C

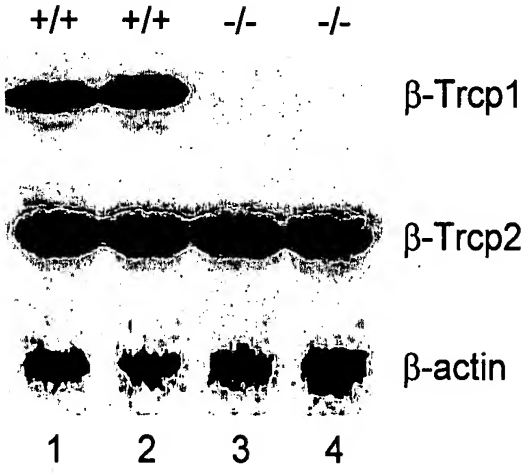


FIG.52D

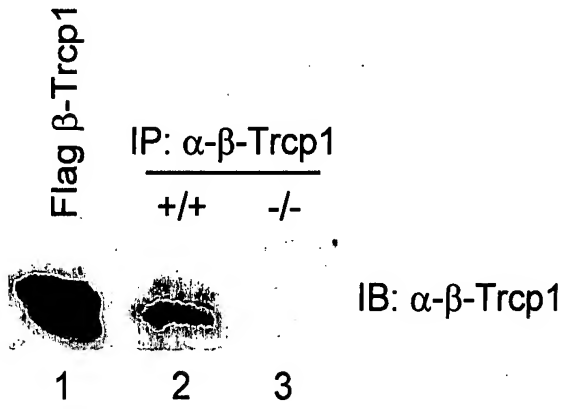


FIG.52E

Docket No.: 5914-099-999
Serial No.: 10/652,928
Inventor(s): Chiaur et al.
Title: METHODS TO IDENTIFY COMPOUNDS USEFUL FOR THE TREATMENT OF PROLIFERATIVE AND DIFFERENTIATIVE DISORDERS

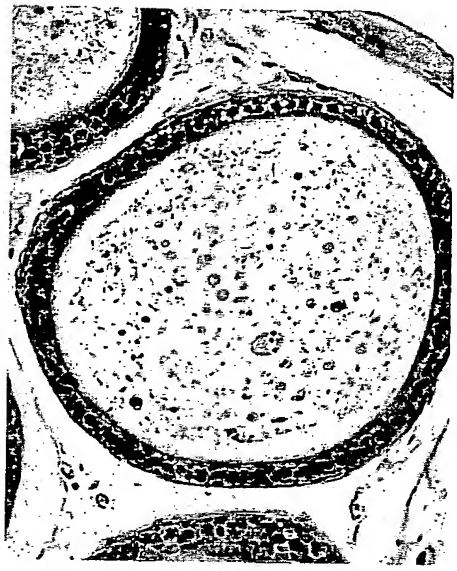


FIG.53B

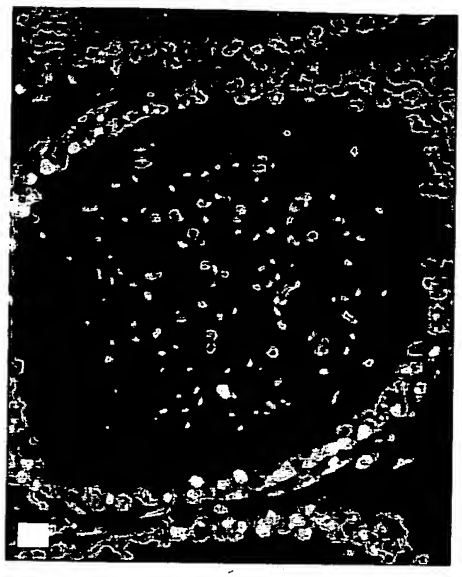


FIG.53D

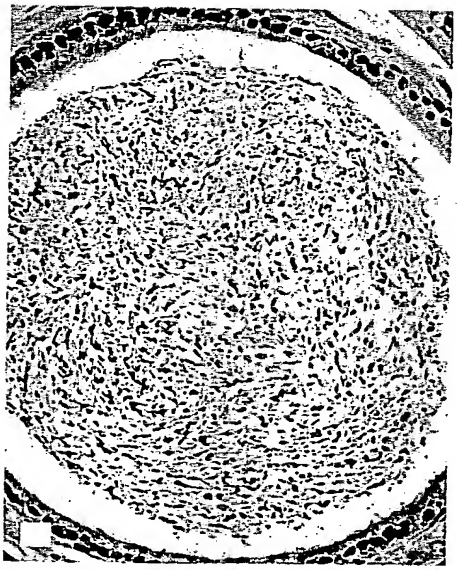


FIG.53A

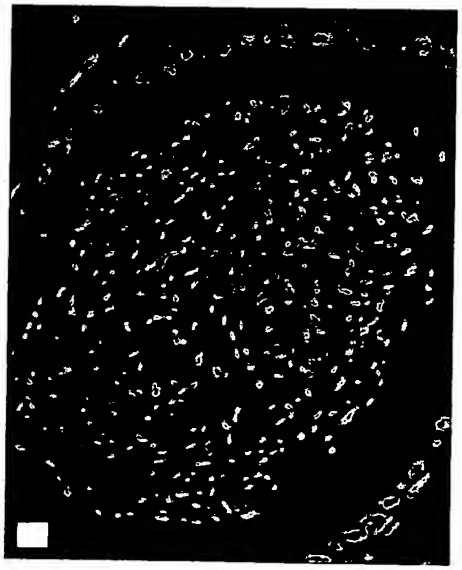


FIG.53C

FIG.53I

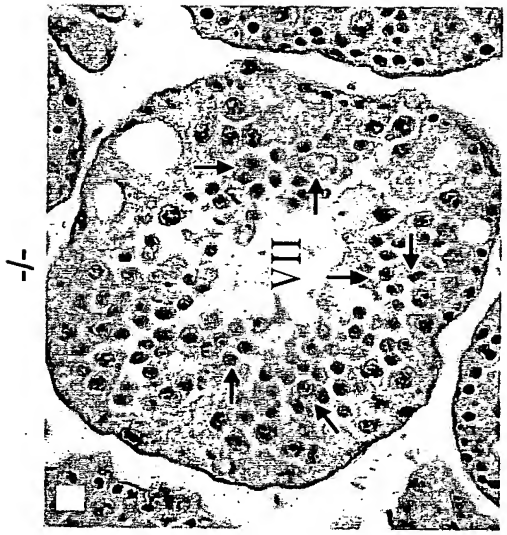


FIG.53F

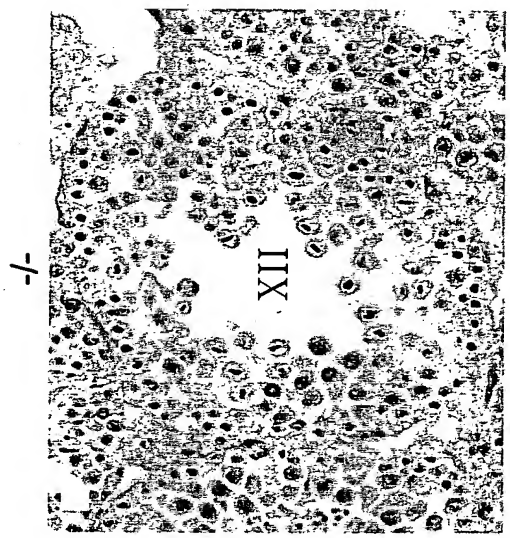


FIG.53H

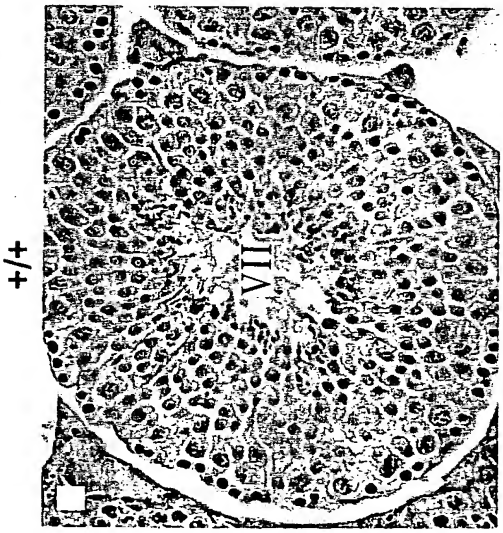


FIG.53E

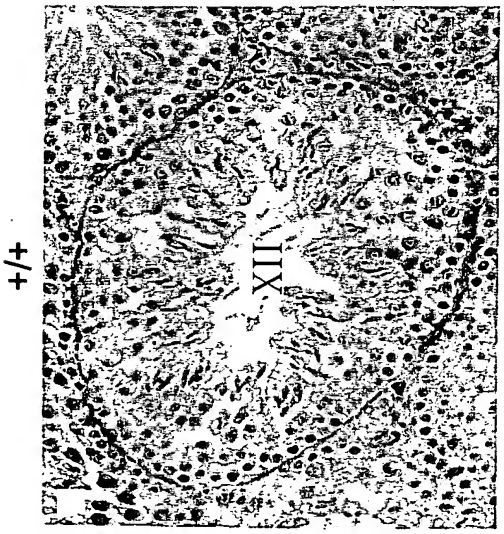


FIG.53G

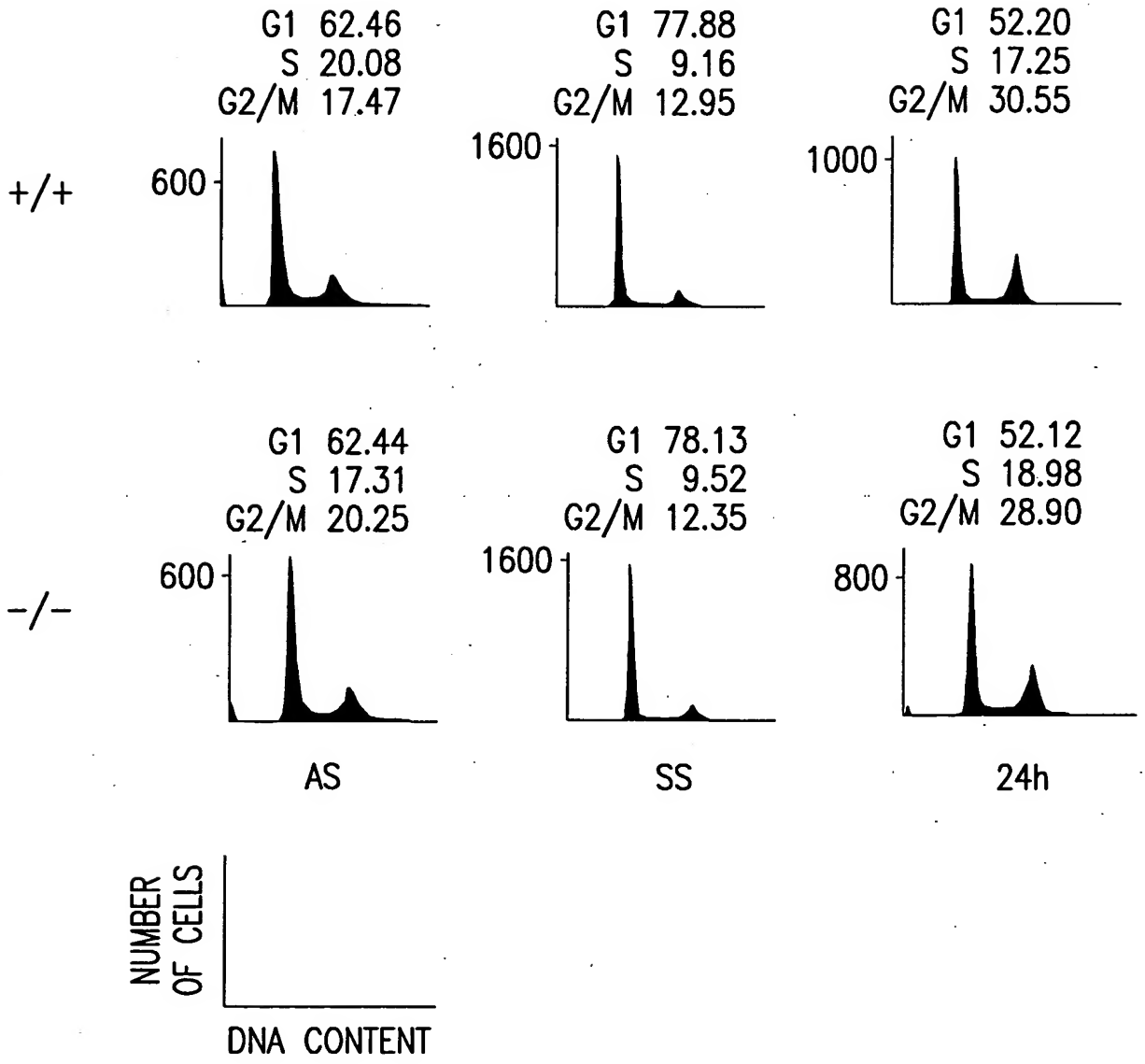

G1 62.46
S 20.08
G2/M 17.47
G1 77.88
S 9.16
G2/M 12.95
G1 52.20
S 17.25
G2/M 30.55
+/+
600
1600
1000
G1 62.44
S 17.31
G2/M 20.25
G1 78.13
S 9.52
G2/M 12.35
G1 52.12
S 18.98
G2/M 28.90
-/-
600
1600
800
AS
SS
24h
NUMBER OF CELLS
DNA CONTENT

FIG.54A

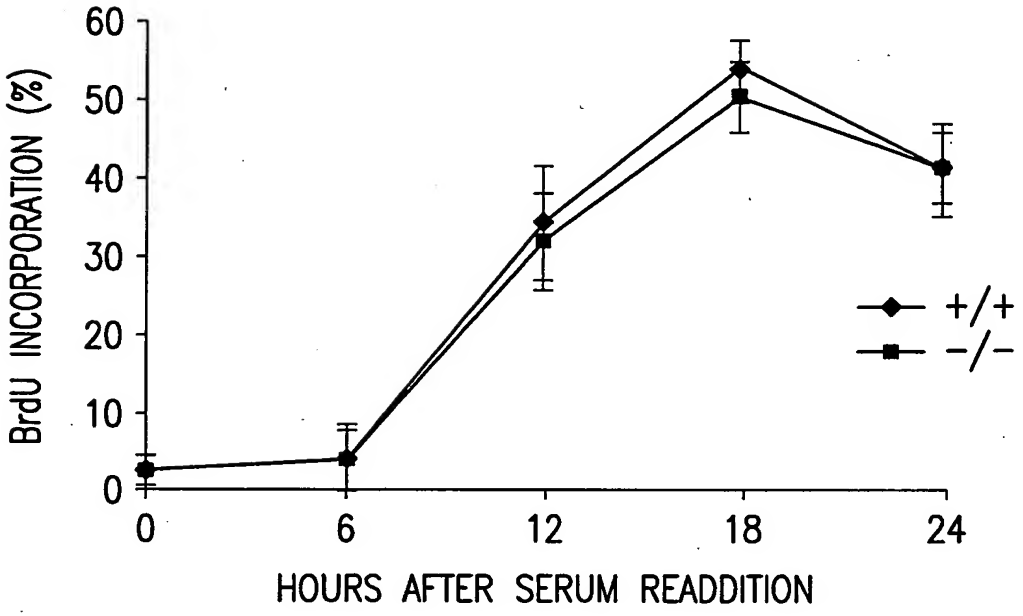

60
50
40
30
20
10
0
BrdU INCORPORATION (%)
0
6
12
18
24
HOURS AFTER SERUM READDITION
+/+
-/-

FIG.54B

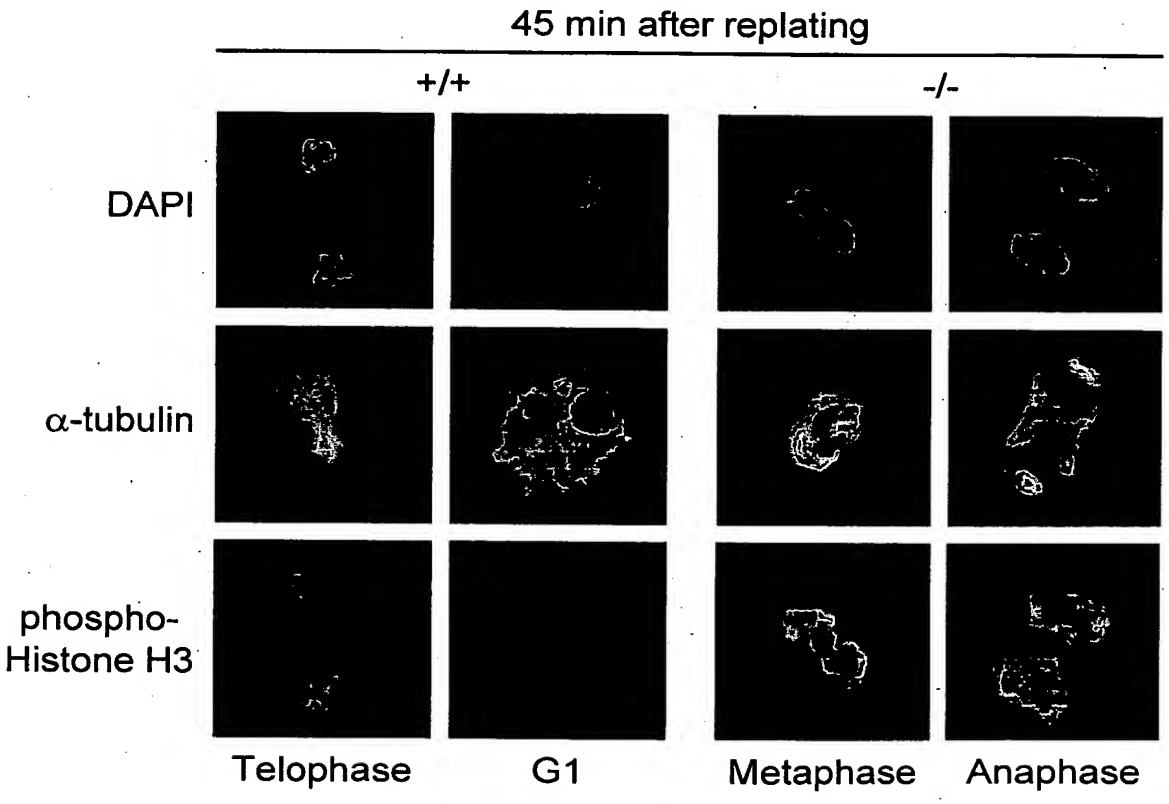

45 min after replating
+/+
-/-
DAPI
α-tubulin
phospho-
Histone H3
Telophase
G1
Metaphase
Anaphase

FIG.54C

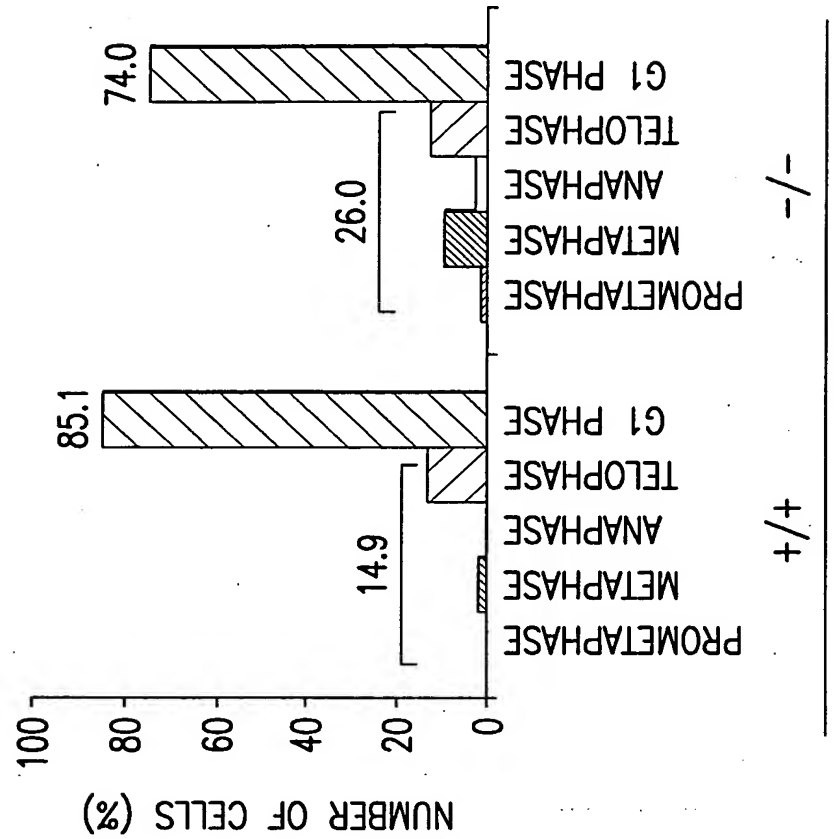


FIG.54D-2

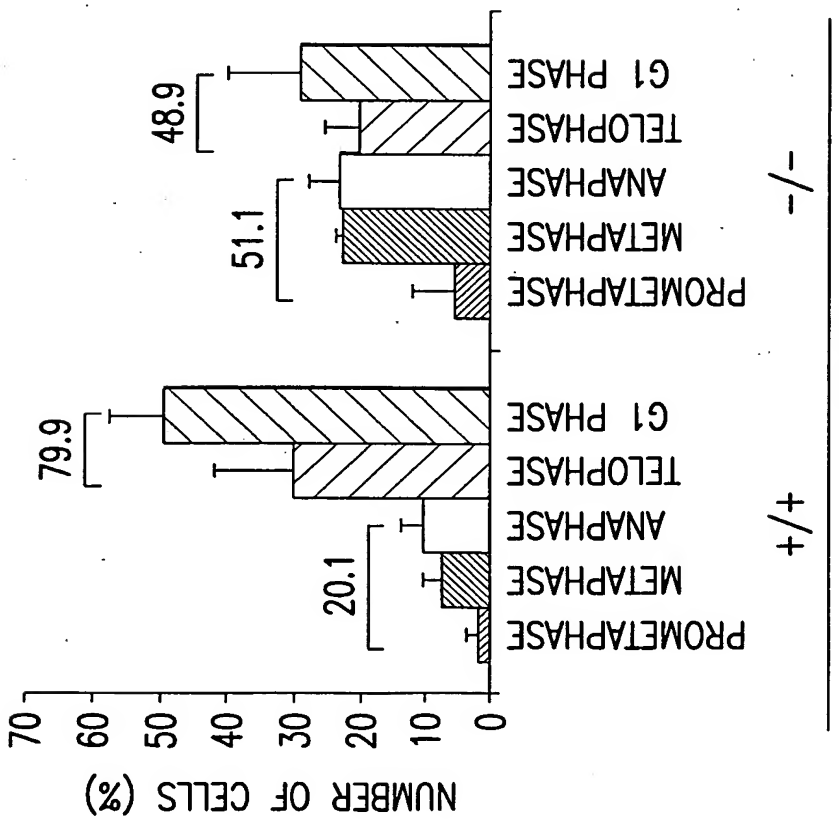


FIG.54D-1

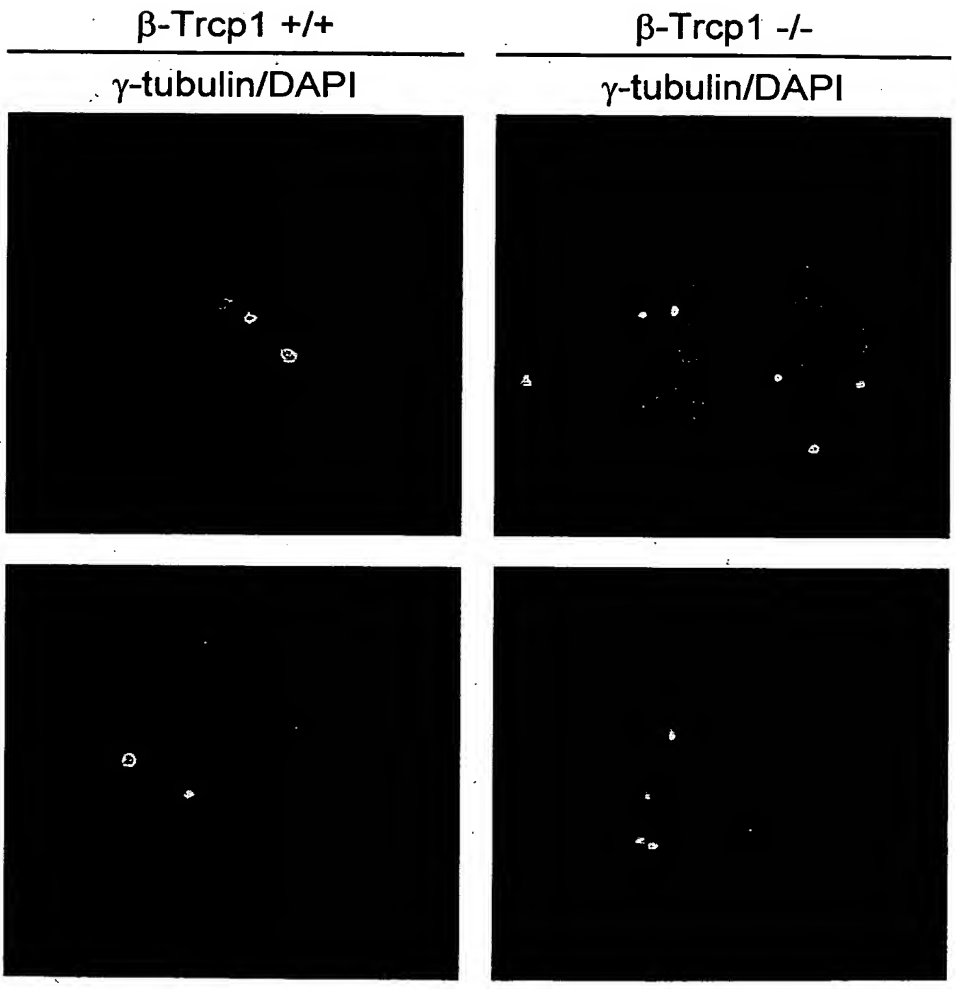


FIG.54E

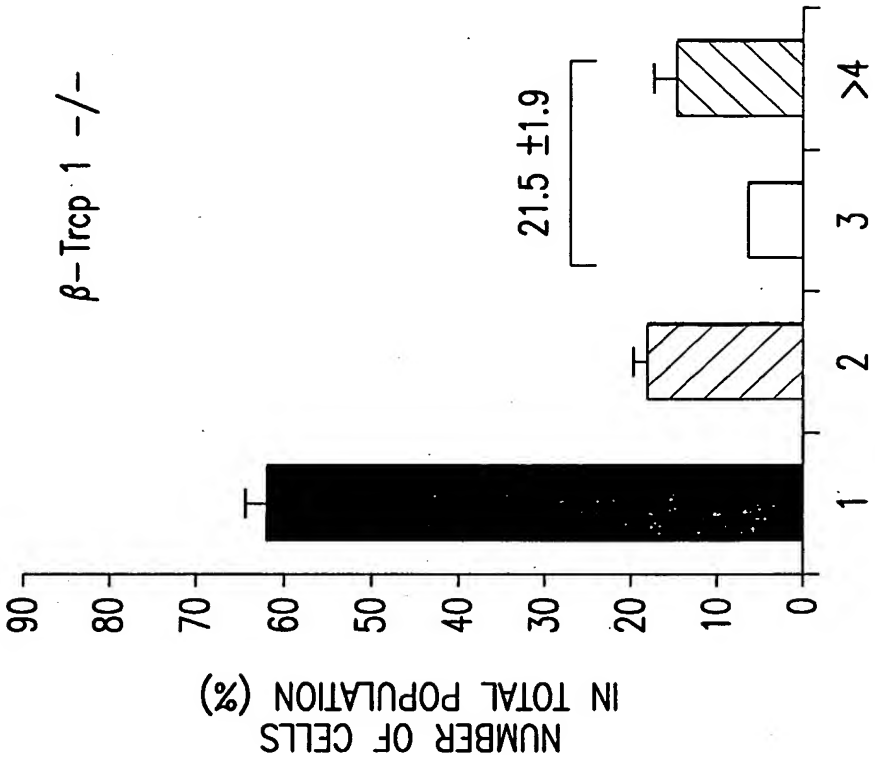


FIG.54F-2

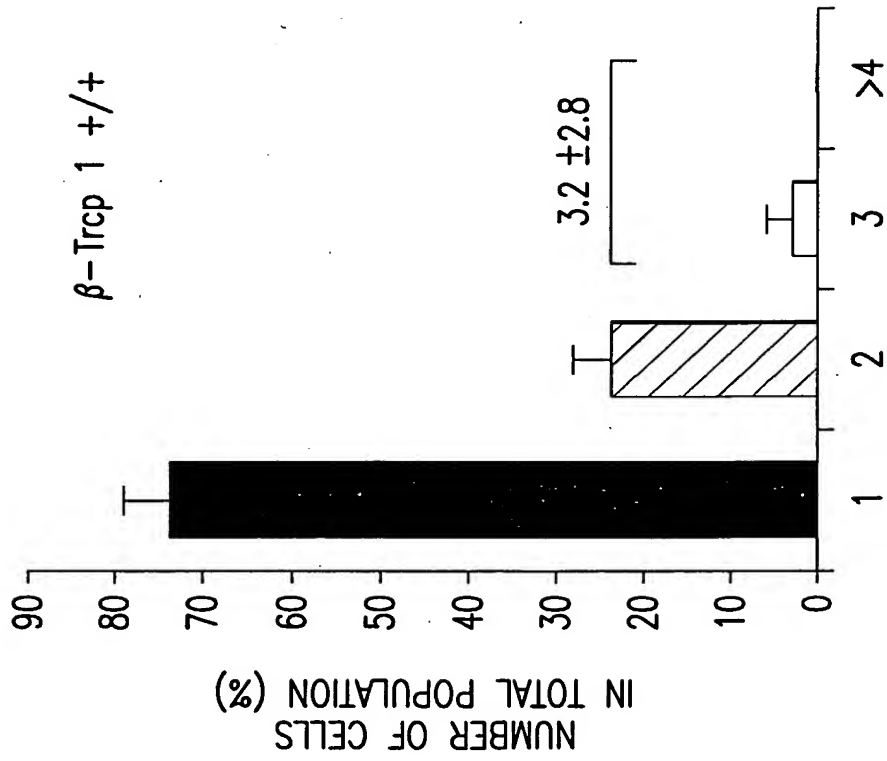


FIG.54F-1

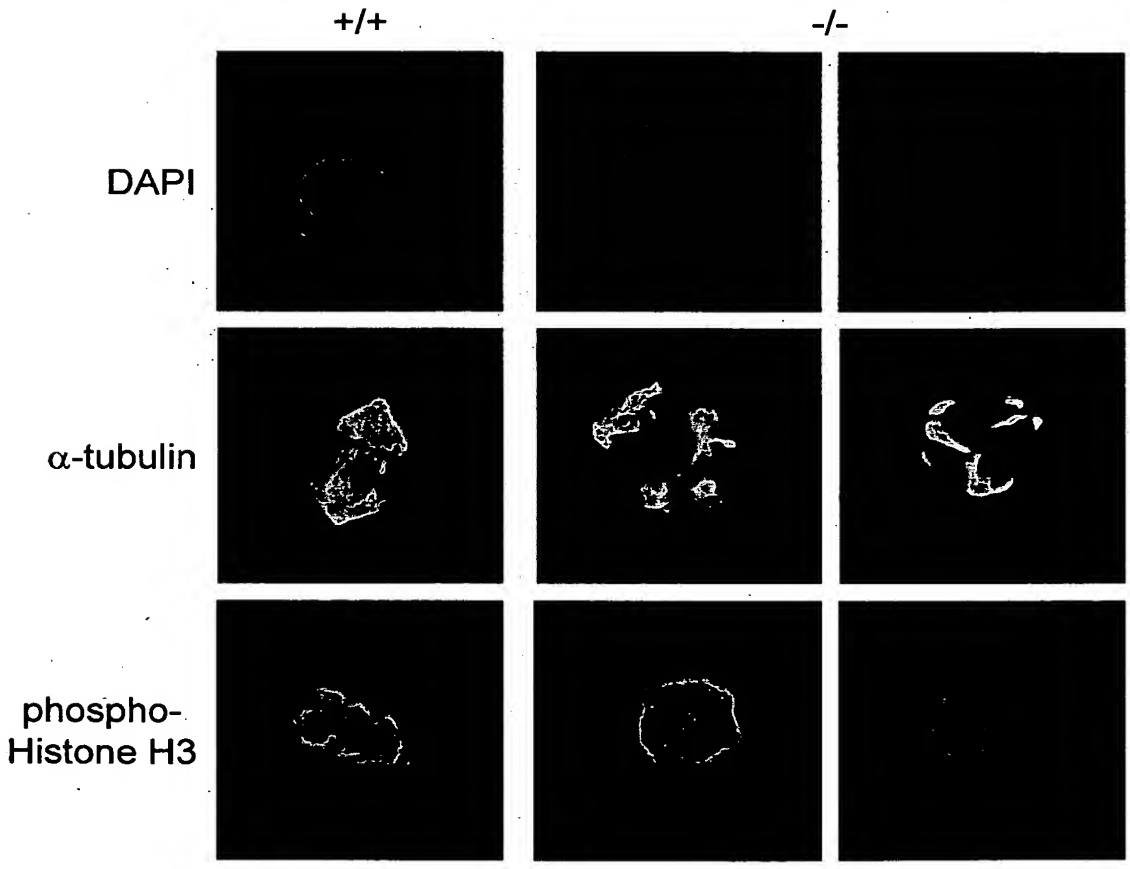


FIG.54G

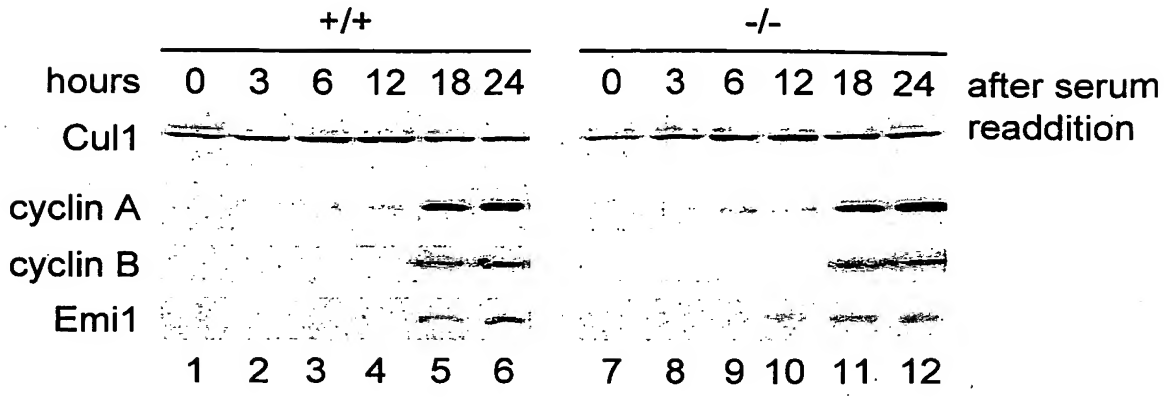


FIG.55A

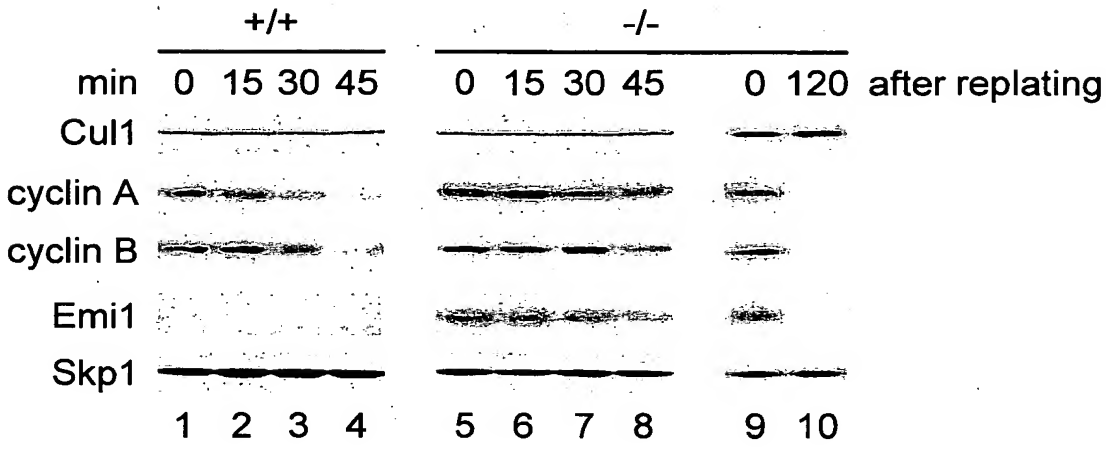


FIG.55B

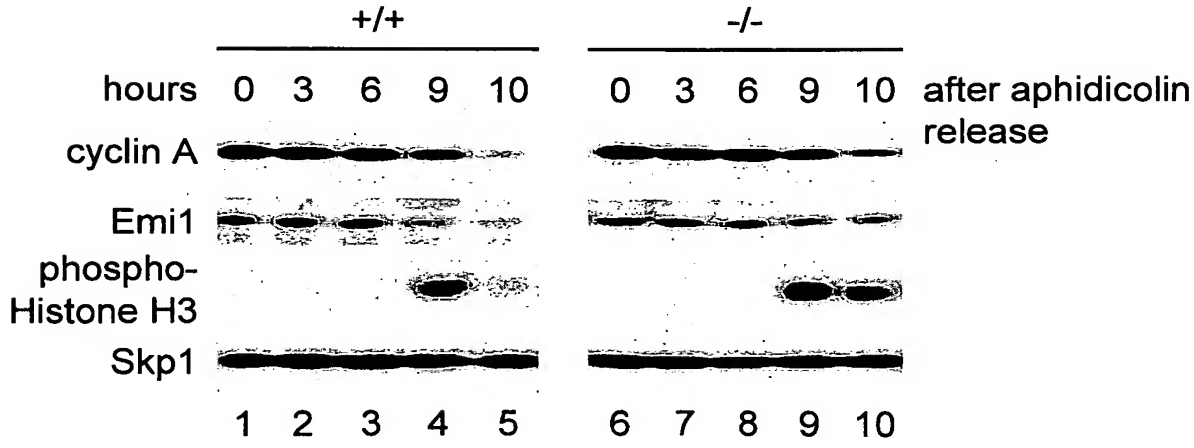


FIG.55C

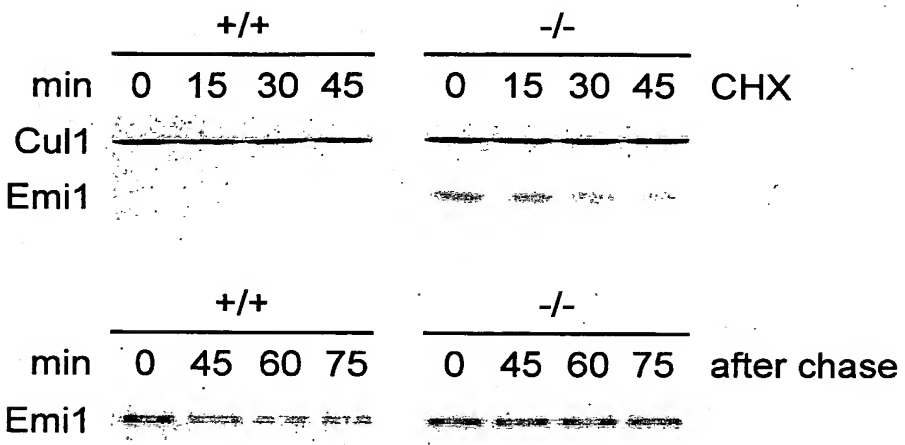


FIG.55D

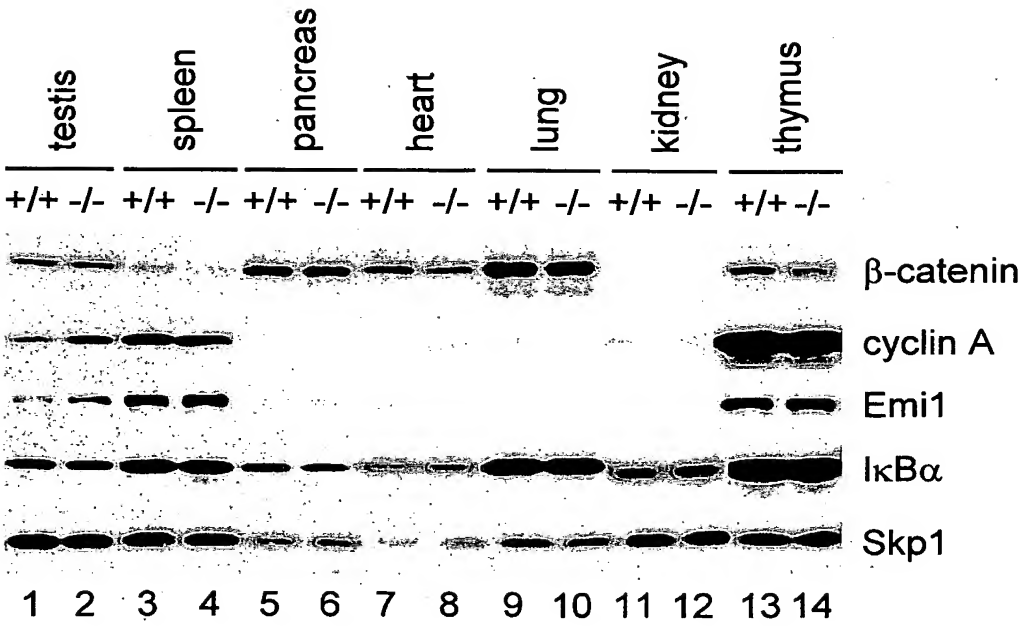


FIG.55E

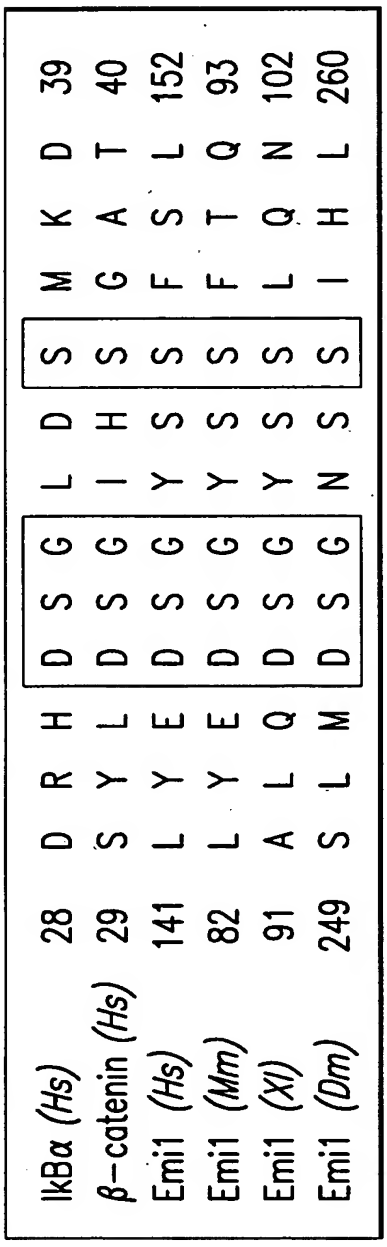

IkBα (Hs) 28 D R H D S G L D S M K D 39
β-catenin (Hs) 29 S Y L D S G I H S G A T 40
Emi1 (Hs) 141 L Y E D S G Y S S F S L 152
Emi1 (Mm) 82 L Y E D S G Y S S F T Q 93
Emi1 (Xl) 91 A L Q D S G Y S S L Q N 102
Emi1 (Dm) 249 S L M D S G N S S I H L 260

FIG.56A

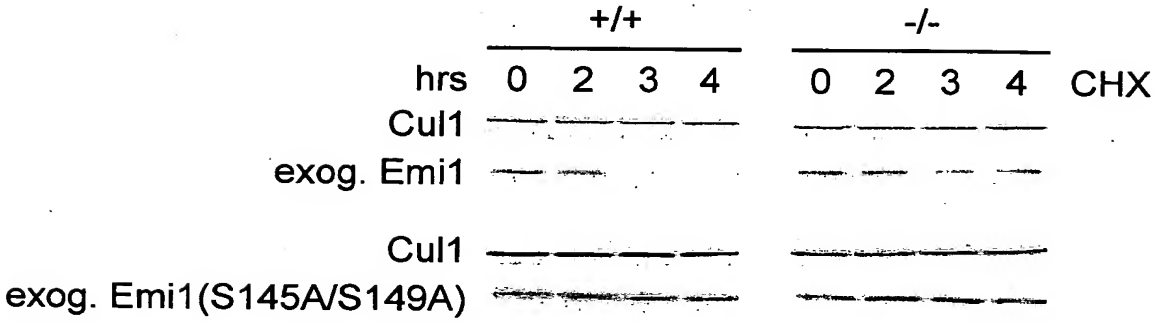


FIG.56B

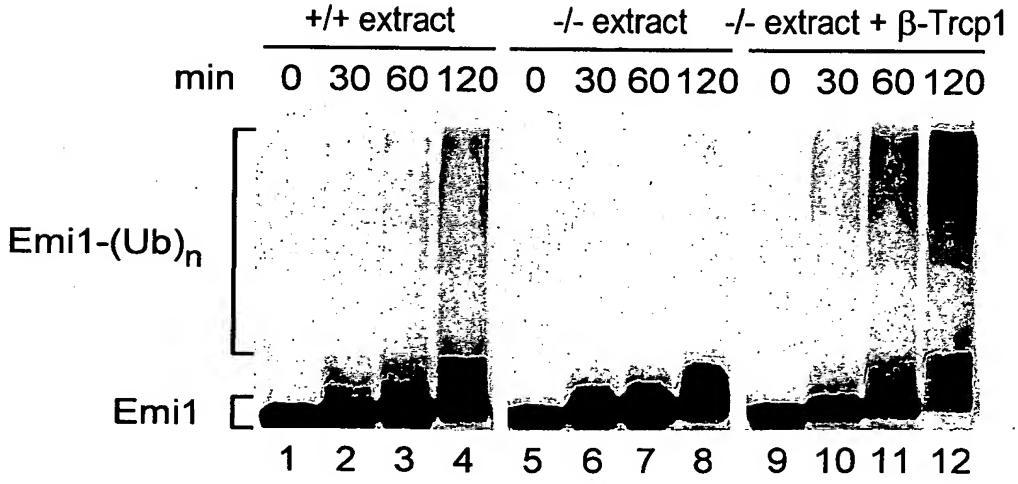


FIG.56C

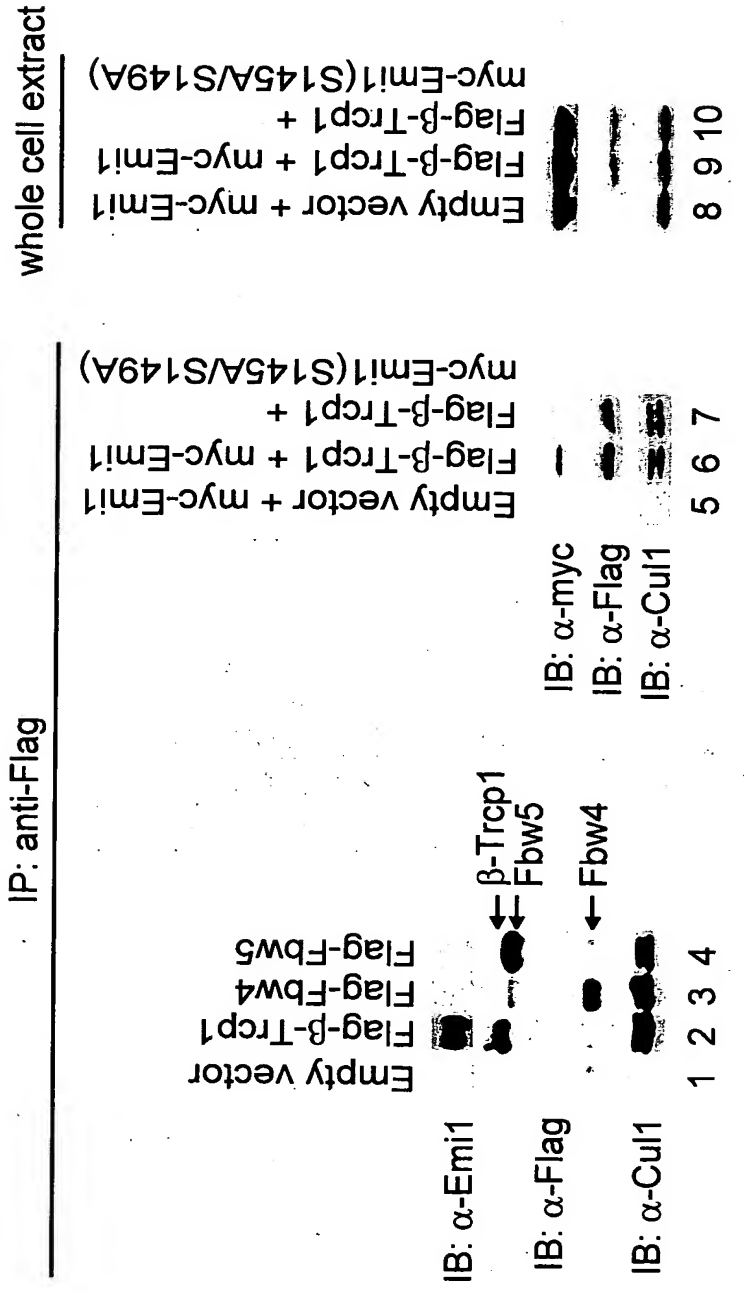

IP: anti-Flag
whole cell extract
IB: α-Emi1
IB: α-Flag
IB: α-Cul1
IB: α-myc
IB: α-Flag
IB: α-Cul1
Empty vector
Flag-β-Trcp1
Flag-Fbw4
Flag-Fbw5
β-Trcp1
Fbw5
Fbw4
Empty vector + myc-Emi1
Flag-β-Trcp1 + myc-Emi1
Flag-β-Trcp1 +
myc-Emi1(S145A/S149A)
Empty vector + myc-Emi1
Flag-β-Trcp1 + myc-Emi1
Flag-β-Trcp1 +
myc-Emi1(S145A/S149A)
1 2 3 4
5 6 7
8 9 10

FIG.56D

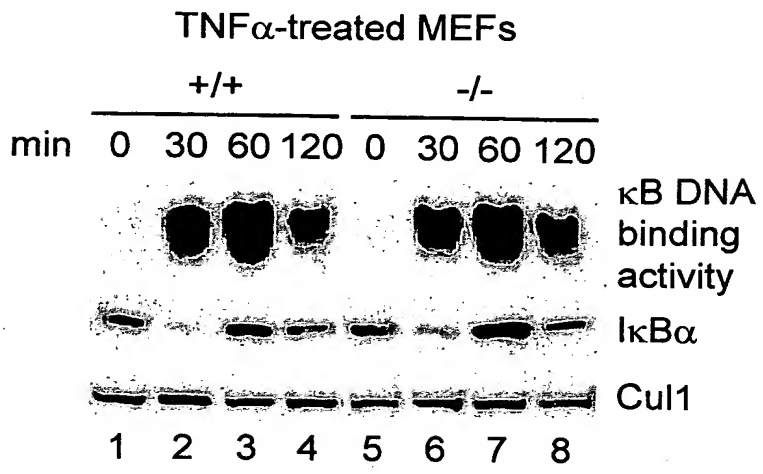


FIG.57A

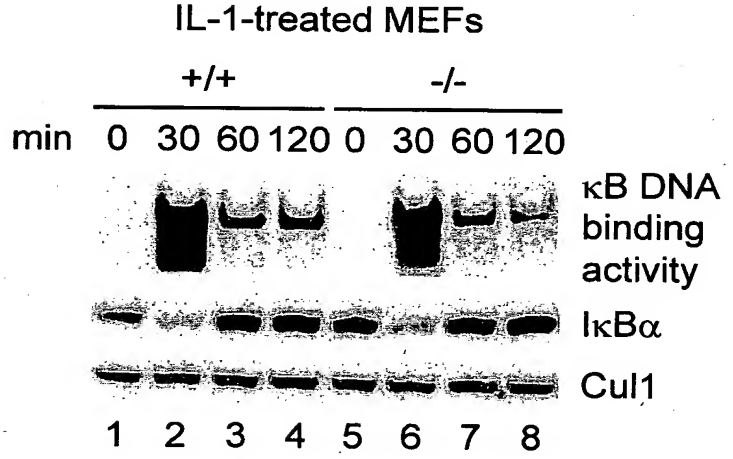


FIG.57B

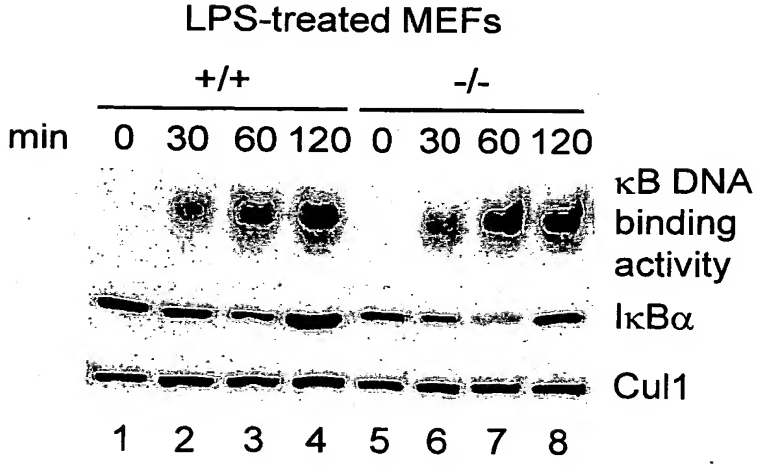


FIG.57C

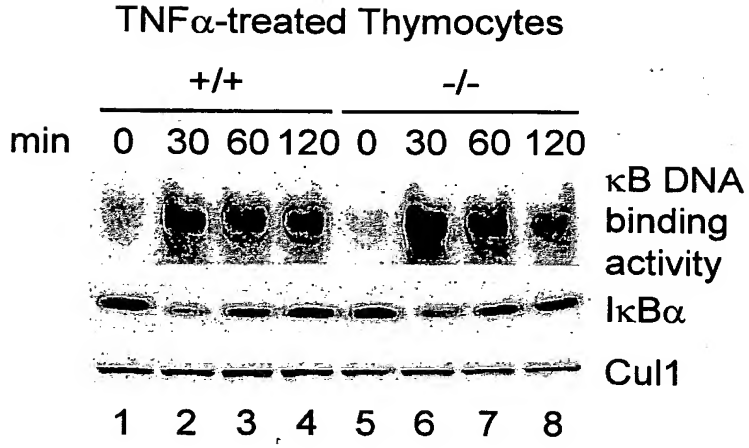


FIG.57D

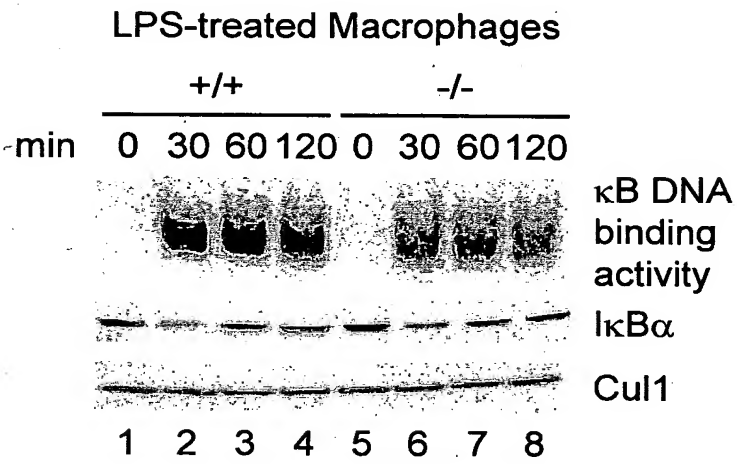


FIG.57E

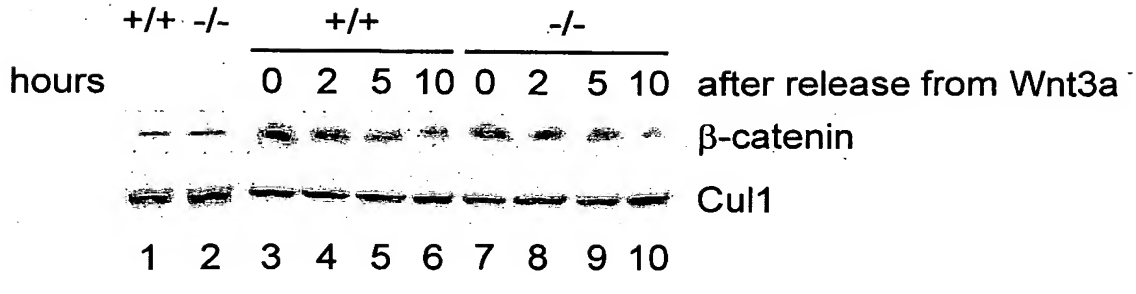


FIG.57F

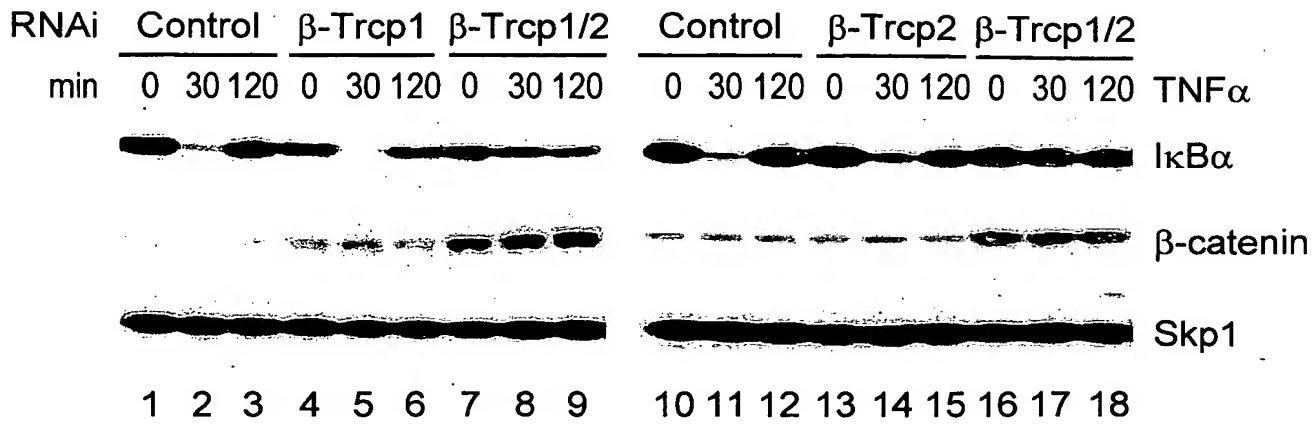


FIG.57G

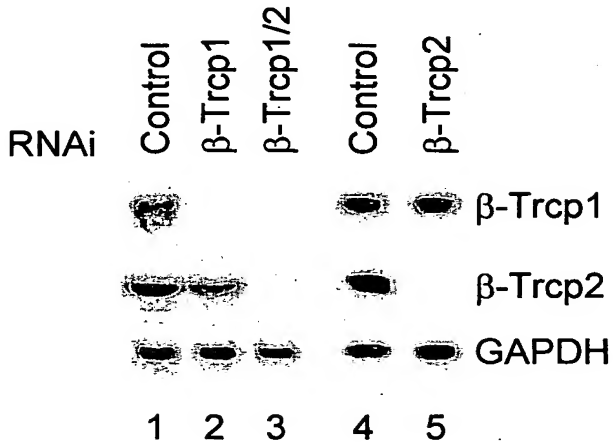


FIG.57H

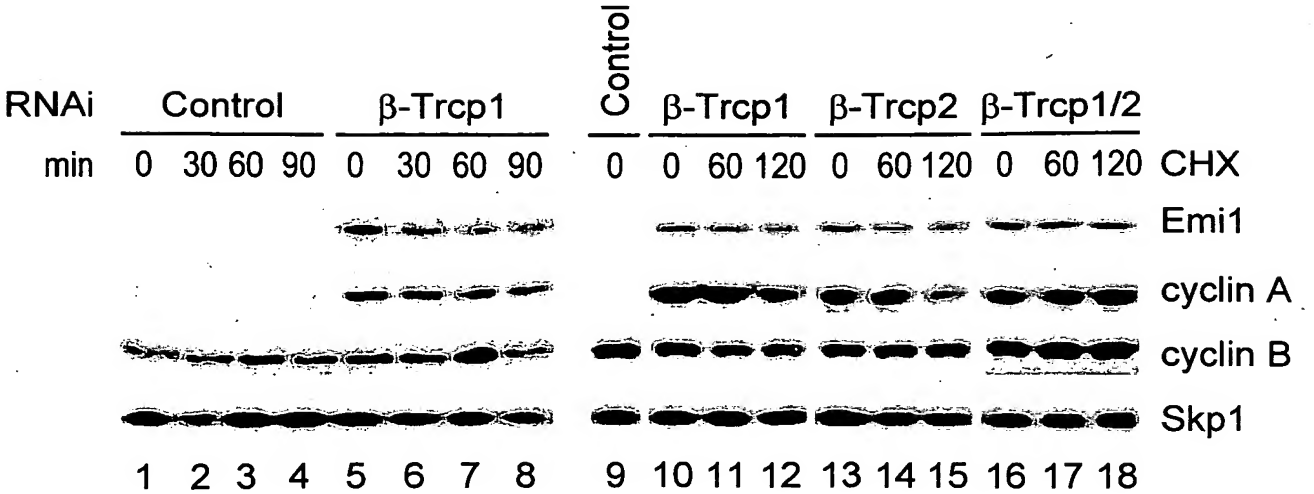


FIG.57I